

Following General Procedure D above using S-(+)-3,5-difluoromandelic acid (Example L) and 3-(L-valinyl)-amino-2,3-dihydro-1-methyl-5-1H-1,4-benzodiazepin-2-one (Example 8-Y), the title compound was prepared as a white solid.

5 $C_{29}H_{28}F_2N_4O_4$ (MW = 534.61); mass spectroscopy found (M+H) 535.3.

Anal. calcd for $C_{29}H_{28}F_2N_4O_4$: C, 65.16; H, 5.28; N, 10.48. Found: C, 65.34; H, 5.43; N, 10.35.

Example 8-13

10 **Synthesis of**
3-[N'-(3,5-Difluorophenyl- α -hydroxyacetyl)-L-*tert*-leucinyl]-amino-
2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one

Following General Procedure D above using S-(+)-3,5-difluoromandelic acid (Example L) and 3-(*tert*-leucinyI)-amino-2,3-dihydro-1-methyl-5-1H-1,4-
15 benzodiazepin-2-one (Example 8-Z), the title compound was prepared as a white solid.

$C_{30}H_{30}F_2N_4O_4$ (MW = 548.64); mass spectroscopy found (M+H) 549.3.

Anal. calcd for $C_{30}H_{30}F_2N_4O_4$: C, 65.68; H, 5.51; N, 10.21. Found: C, 65.38; H, 5.44; N, 10.14.

Example 8-14

Synthesis of
3-[N'-(3,5-Difluorophenylacetyl)-L-alaninyl]-amino-
2,3-dihydro-1-methyl-5-(3-fluorophenyl)-1H-1,4-benzodiazepin-2-one

25 Following General Procedure D above using 3,5-difluorophenylacetic acid (Oakwood Products, Inc.) and 3-(L-alaninyl)-amino-2,3-dihydro-1-methyl-5-(3-fluorophenyl)-1H-1,4-benzodiazepin-2-one (Example 8-J), the title compound was prepared as an off white solid.

$C_{27}H_{23}F_3N_4O_3$ (MW = 508.50); mass spectroscopy found (M+H) 509.3.

30 ¹H NMR (300 MHz, CDCl₃): δ = 7.65-7.53 (4H, m), 7.42-7.24 (12H, m), 7.22-7.14 (2H, m), 6.87-6.81 (4H, m), 6.75-6.65 (2H, m), 6.29 (1H, d, J=6.6 Hz), 6.21 (1H, d, J=7.2 Hz), 5.45 (1H, d, J=7.8 Hz), 5.44 (1H, d, J=7.5

Hz), 4.67 (2H, m), 3.57 (2H, s), 3.55 (2H, s), 3.474 (3H, s), 3.468 (3H, s), 1.48 (3H, d, J=7.2 Hz), 1.47 (3H, d, J=6.8 Hz).

Example 8-15

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Synthesis of 3-[N'-(3,5-Difluorophenylacetyl)-L-alaninyl]amino- 2,3-dihydro-1-methyl-5-(4-fluorophenyl)-1H-1,4-benzodiazepin-2-one

Following General Procedure D above using 3,5-difluorophenylacetic acid (Oakwood Products, Inc.) and 3-(L-alaninyl)-amino-2,3-dihydro-1-methyl-5-(4-fluorophenyl)-1H-1,4-benzodiazepin-2-one (Example 8-K), the title compound was prepared as an off-white solid.

$C_{27}H_{23}F_3N_4O_3$ (MW = 508.50); mass spectroscopy found (M+H) 509.7.

Anal. calcd for $C_{27}H_{23}F_3N_4O_3$: C, 63.78; H, 4.56; N, 11.01. Found: C, 64.09; H, 4.81; N, 10.40.

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Example 8-16

Synthesis of 3-[N'-(Cyclopentyl- α -hydroxyacetyl)-L-alaninyl]-amino- 2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one

Following General Procedure D above using (\pm)- α -hydroxy-cyclopentylacetic acid (Example P) and 3-(L-alaninyl)-amino-2,3-dihydro-1-methyl-5-1H-1,4-benzodiazepin-2-one (Example 8-B), the title compound was prepared as a white solid.

Isomer 1:

25 $C_{26}H_{30}N_4O_4$ (MW = 462.60); mass spectroscopy found (M+H) 463.6.

Anal. calcd for $C_{26}H_{30}N_4O_4$: C, 67.51; H, 6.54; N, 12.11. Found: C, 67.78; H, 6.65; N, 12.29.

Isomer 2:

$C_{26}H_{30}N_4O_4$ (MW = 462.60); mass spectroscopy found (M+H) 463.4.

30 Anal. calcd for $C_{26}H_{30}N_4O_4$: C, 67.51; H, 6.54; N, 12.11. Found: C, 67.74; H, 6.56; N, 11.81.

Example 8-17

Synthesis of
3-[N'-(Cyclopentyl- α -hydroxyacetyl)-L-valinyl]-amino-
2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one

5 Following General Procedure D above using (\pm)- α -hydroxy-
cyclopentylacetic acid (Example P) and 3-(L-valinyl)-amino-2,3-dihydro-1-
methyl-5-1H-1,4-benzodiazepin-2-one (Example 8-B), the title compound was
prepared as a white solid.

Isomer 1:

10 $C_{28}H_{34}N_4O_4$ (MW = 490.66); mass spectroscopy found (M+H) 491.4.

Isomer 2:

$C_{28}H_{34}N_4O_4$ (MW = 490.66); mass spectroscopy found (M+H) 491.4.

Example 8-18

15 Synthesis of
3-[N'-(3,5-Difluorophenylacetyl)-L-alaninyl]amino-
2,3-dihydro-1,5-dimethyl-1H-1,4-benzodiazepin-2-one

Following General Procedure D above using 3,5-difluorophenylacetic acid
(Oakwood Products, Inc.) and 3-(L-alaninyl)-amino-2,3-dihydro-1,5-dimethyl-
20 1H-1,4-benzodiazepin-2-one (Example 8-AA), the title compound was prepared
as a solid (mp. = 222-223°C). The product was purified by slurrying in ether.

MW = 429; mass spectroscopy found (M+H) 429.

Anal. calcd: C, 61.67; H, 5.18; N, 13.08. Found: C, 61.43; H, 5.17;
N, 12.79.

25 Example 8-19

Synthesis of
3-[N'-(3,5-Difluorophenylacetyl)-L-alaninyl]amino-
2,3-dihydro-1-isobutyl-5-phenyl-1H-1,4-benzodiazepin-2-one

30 Following General Procedure D above using 3,5-difluorophenylacetic acid
(Oakwood Products, Inc.) and 3-(L-alaninyl)-amino-2,3-dihydro-1-isobutyl-5-
phenyl-1H-1,4-benzodiazepin-2-one (Example 8-L), the title compound was

prepared as a solid (mp. = 210-211°C). The product was purified by titration from ether/hexanes.

$C_{30}H_{30}F_2N_4O_3$ (MW = 532.23); mass spectroscopy found (M+H) 532.

Anal. calcd: C, 67.66; H, 5.68; N, 10.52. Found: C, 67.67; H, 5.55;
5 N, 10.34.

Purification by C 2000 chromatography, eluting with hexanes/ethyl acetate (20:80) afforded the following isomers:

Isomer 1:

Melting Point: 202-203°C.

10 $C_{30}H_{30}F_2N_4O_3$ (MW = 532.23); mass spectroscopy found (M+H) 532.23.

Isomer 2:

Melting Point: 211-212°C.

$C_{30}H_{30}F_2N_4O_3$ (MW = 532.23); mass spectroscopy found (M+H) 532.

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Example 8-20

Synthesis of

3-[N'-(3,5-Difluorophenyl- α -hydroxyacetyl)-L-alaninyl]amino- 2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one

Following General Procedure D above using 3,5-difluoromandelic acid
20 (Fluorochem) and 3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B), the title compound was prepared as a solid. The product was purified by LC 2000 chromatography, eluting with hexanes/ethyl acetate (20:80).

Isomer 1:

25 Melting Point: 240-241°C.

$C_{27}H_{24}F_2N_4O_4$ (MW = 506.51); mass spectroscopy found (M+H) 506.

Anal. calcd for $C_{27}H_{24}F_3N_4O_4$: C, 64.03; H, 4.78; N, 11.06. Found: C,
64.31; H, 4.86; N, 11.04.

Isomer 2:

30 Melting Point: 128°C.

$C_{27}H_{24}F_2N_4O_4$ (MW = 506.51); mass spectroscopy found (M+H) 506.

Anal. calcd for $C_{27}H_{24}F_3N_4O_4$: C, 64.03; H, 4.78; N, 11.06. Found: C, 63.92; H, 5.00; N, 10.88.

Example 8-21

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Synthesis of 3-[N'-(3,5-Difluorophenyl- α -oxoacetyl)-L-alaninyl]amino- 2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one

Following General Procedure D above using 3,5-difluoro- α -oxoacetic acid (Example O) and 3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B), the title compound was prepared as a solid (mp. = 128-129°C). The product was purified by LC 2000 chromatography, eluting with hexanes/ethyl acetate (30:70).

$C_{27}H_{22}F_2N_4O_4$ (MW = 504); mass spectroscopy found (M+H) 503.9.

Optical Rotation: $[\alpha] = -113.64 @ 589; -333.33 @ 365$ (c 1, MeOH).

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Anal. calcd for $C_{27}H_{22}F_2N_4O_4$: C, 64.28; H, 4.40; N, 11.11. Found: C, 64.51; H, 4.54; N, 11.04.

Example 8-22

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Synthesis of 3-[N'-(2-Methylthioacetyl)-L-alaninyl]amino- 2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one

Following General Procedure D above using 2-methylthioacetic acid (Aldrich) and 3-(L-alaninyl)-amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B), the title compound was prepared as a solid (mp. = 205-206°C). The product was purified by slurrying in hexanes/ether (1:1).

25

$C_{22}H_{24}N_4O_3S$ (MW = 424); mass spectroscopy found (M+H) 424.

Anal. calcd for $C_{22}H_{24}N_4O_3S$: C, 62.25; H, 5.70; N, 13.20. Found: C, 62.11; H, 5.89; N, 13.02.

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Example 8-23

Synthesis of
3-[N'-(3,5-Difluorophenylacetyl)-L-valinyl]amino-
2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one

5 Following General Procedure D above using 3,5-difluorophenylacetic acid (Oakwood Products, Inc.) and 3-(L-valinyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-Y), the title compound was prepared as a solid (mp. = 228-229°C). The product was purified by slurrying in ether/hexanes (80:20).

10 $C_{29}H_{28}F_2N_4O_3$ (MW = 518); mass spectroscopy found (M+H) 518.

Optical Rotation: $[\alpha] = -117.96 @ 589; -341.55 @ 365$ (c 1, MeOH).

Anal. calcd for $C_{29}H_{28}F_2N_4O_3$: C, 67.17; H, 5.44; N, 10.8. Found: C, 67.45; H, 5.49; N, 10.61.

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Example 8-24

Synthesis of
3-[N'-(3,5-Difluorophenylacetyl)-L-tert-leucinyl]amino-
2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one

20 Following General Procedure D above using 3,5-difluorophenylacetic acid (Oakwood Products, Inc.) and 3-(L-tert-leucinyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-Z), the title compound was prepared as a solid (mp. = 221-222°C). The product was purified by slurrying in ether.

$C_{30}H_{30}F_2N_4O_3$ (MW = 532); mass spectroscopy found (M+H) 532.

25 Anal. calcd for $C_{30}H_{30}F_2N_4O_3$: C, 67.66; H, 5.68; N, 10.52. Found: C, 67.93; H, 5.95; N, 10.25.

Example 8-25

Synthesis of
3-[N'-(3,5-Difluorophenylacetyl)-L-alaninyl]amino-
2,3-dihydro-1-isopropyl-5-phenyl-1H-1,4-benzodiazepin-2-one

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Following General Procedure D above using 3,5-difluorophenylacetic acid (Oakwood Products, Inc.) and 3-(L-alaninyl)amino-2,3-dihydro-1-isopropyl-5-

phenyl-1H-1,4-benzodiazepin-2-one (Example 8-L), the title compound was prepared as a solid (mp. = 208-209°C). The product was purified by slurrying in ether/hexanes (1:1).

MW = 518; mass spectroscopy found (M+H) 518.

Anal. calcd: C, 67.17; H, 5.44; N, 10.80. Found: C, 67.39; H, 5.62; N, 10.84.

Example 8-26

Synthesis of 3-[N'-(3,5-Difluorophenylacetyl)-L-alaninyl]amino- 2,3-dihydro-1-cyclopropylmethyl-5-phenyl-1H-1,4-benzodiazepin-2-one

Following General Procedure D above using 3,5-difluorophenylacetic acid (Oakwood Products, Inc.) and 3-(L-alaninyl)amino-2,3-dihydro-1-cyclopropylmethyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-L), the title compound was prepared as a solid (mp. = 203-205°C). The product was purified by slurrying in ether/hexanes.

$C_{30}H_{28}F_2N_4O_3$ (MW = 530.58); mass spectroscopy found (M+H) 530.

Anal. calcd for $C_{30}H_{28}F_2N_4O_3$: C, 67.91; H, 5.32; N, 10.56. Found: C, 68.14; H, 5.54; N, 10.62.

Example 8-27

Synthesis of 3-[N'-(3,5-Difluorophenyl- α -fluoroacetyl)-L-alaninyl]amino- 2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one

Following General Procedure D above using 3,5-difluorophenyl- α -fluoroacetic acid (Example S) and 3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-Y), the title compound was prepared as a solid. The product was purified by LC 2000 chromatography, eluting with hexanes/ethyl acetate (35:65).

Isomer 1:

Melting Point: 119-120°C.

$C_{27}H_{23}F_3N_4O_3$ (MW = 508); mass spectroscopy found (M+H) 508.

Optical Rotation: $[\alpha] = -115.62 @ 589; -292.09 @ 365$ (c 1, MeOH).

Anal. calcd for $C_{27}H_{23}F_3N_4O_3$: C, 62.66; H, 4.67; N, 10.82. Found: C, 62.55; H, 4.74; N, 10.51.

Isomer 2:

Melting Point: 198-199°C.

5 $C_{27}H_{23}F_3N_4O_3$ (MW = 508); mass spectroscopy found (M+H) 508.

Optical Rotation: $[\alpha] = -99.65 @ 589; -279.72 @ 365$ (c 1, MeOH).

Anal. calcd for $C_{27}H_{23}F_3N_4O_3$: C, 62.66; H, 4.67; N, 10.82. Found: C, 62.40; H, 4.62; N, 10.84.

10

Examples 8-28 to 8-139

By following the procedures set forth above, the following additional compounds were prepared:

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|----|------|---|
| 15 | 8-28 | 3-[N'-(3,5-difluorophenylacetyl)-L-alaninyl]amino-2,3-dihydro-1- <i>n</i> -propyl-5-phenyl-1H-1,4-benzodiazepin-2-one |
| | 8-29 | 3-[N'-(3-methylbutyryl)-L-phenylglycinyl]amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one |
| 20 | 8-30 | 3-[N'-(3,5-difluorophenylacetyl)-L-phenylglycinyl]amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one |
| | 8-31 | 3-[N'-(2-phenylthioacetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one |
| 25 | 8-32 | 3-[N'-(3-methylbutyryl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one |
| | 8-33 | 3-[N'-(2-phenylthioacetyl)-L-phenylglycinyl]amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one |
| 30 | 8-34 | 3-[N'-(3-(4-methoxyphenyl)propionyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one |
| 35 | 8-35 | 3-[N'-(3-bromophenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one |
| | 8-36 | 3-[N'-(4-cyclohexylbutyryl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one |
| 40 | | |

	8-37	3-[N'-(4-methoxyphenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
5	8-38	3-[N'-(3-methyl-2-hydroxybutyryl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one
	8-39	3-[N'-(3-methyl-2-hydroxybutyryl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one
10	8-40	3-[N'-(3,3-dimethylbutyryl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one
	8-41	3-[N'-(thien-2-yl-acetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
15	8-42	3-[N'-(3,5-difluorophenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
20	8-43	3-[N'-(3-bromophenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
	8-44	3-[N'-(2-phenylthioacetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
25	8-45	3-[N'-(4-ethoxyphenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
	8-46	3-[N'-(4-trifluoromethylphenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
30	8-47	3-[N'-(3,5-di(trifluoromethyl)phenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
35	8-48	3-[N'-(2-methylthioacetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
	8-49	3-[N'-(2-cyclohexylacetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
40	8-50	3-[N'-(2,3,4,5,6-pentafluorophenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
45	8-51	3-[N'-(thionaphth-3-ylacetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one

	8-52	3-[N'-(2,4,6-trimethylphenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
5	8-53	3-[N'-((4-phenyl)phenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
	8-54	3-[N'-(3,4-difluorophenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
10	8-55	3-[N'-(4-(thien-2-yl)butyryl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
	8-56	3-[N'-(5-methylhexanoyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
15	8-57	3-[N'-(2-methoxycarbonylacetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
20	8-60	3-[N'-(2,6-difluorophenyl)- α -hydroxyacetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
	8-61	3-[N'-(4-fluorophenyl)- α -hydroxyacetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
25		
	8-62	3-[N'-(2,5-difluorophenyl)- α -hydroxyacetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
30		
	8-63	3-[N'-(2,4,6-trifluorophenyl)acetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
	8-64	3-[N'-(2-trifluoromethyl-4-fluorophenyl)acetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
35		
	8-65	3-[N'-(4,4,4-trifluorobutyryl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
40		
	8-66	3-[N'-(4- <i>iso</i> -propylphenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
	8-67	3-[N'-(3-phenyl-2-hydroxypropionyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
45		

	8-68	3-[N'-(phenyl- α -hydroxyacetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
5	8-69	3-[N'-(4-chlorophenyl- α -hydroxyacetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
10	8-70	3-[N'-(3-methylbutyryl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
	8-71	3-[N'-(2,3,5-trifluorophenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
15	8-72	3-[N'-(3-methylthiopropionyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
	8-73	3-[N'-(3-methyl-2-hydroxybutyryl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
20	8-74	3-[N'-(3-nitrophenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
25	8-75	3-[N'-(4-methoxyphenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
30	8-76	3-[N'-(2-thienylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
	8-77	3-[N'-(3,5-difluorophenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
35	8-78	3-[N'-(3-bromophenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
40	8-79	3-[N'-(2-phenylthioacetyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
45	8-80	3-[N'-(4-ethoxyphenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one

	8-81	3-[N'-(4-trifluoromethylphenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
5	8-82	3-[N'-(3,5-di-(trifluoromethyl)phenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
10	8-83	3-[N'-(2-methylthioacetyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
15	8-84	3-[N'-(2-cyclomethylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
20	8-85	3-[N'-(2,3,4,5,6-pentafluorophenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
	8-86	3-[N'-(thionaphth-3-ylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
25	8-87	3-[N'-(2,4,6-trimethylphenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
30	8-88	3-[N'-((4-phenyl)phenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
35	8-89	3-[N'-(3,4-difluorophenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
40	8-90	3-[N'-(4-(2-thienyl)butyryl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
	8-91	3-[N'-(5-methylhexanoyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one

	8-95	3-[N'-(2,6-difluorophenyl- α -hydroxyacetyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
5	8-96	3-[N'-(4-fluorophenyl- α -hydroxyacetyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
10	8-97	3-[N'-(2,5-difluorophenyl- α -hydroxyacetyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
15	8-98	3-[N'-(2,4,6-trifluorophenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
20	8-99	3-[N'-(2-trifluoromethyl-4-fluorophenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
	8-100	3-[N'-(4,4,4-trifluorobutyryl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
25	8-101	3-[N'-(4- <i>iso</i> -propylphenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
30	8-102	3-[N'-(3-phenyl-2-hydroxypropionyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
35	8-103	3-[N'-(phenyl- α -hydroxyacetyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
	8-104	3-[N'-(4-chlorophenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
40	8-105	3-[N'-(3-methylbutyryl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one

	8-106	3-[N'-(2,3,5-trifluorophenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
5	8-107	3-[N'-(3-methylthiopropionyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
10	8-108	3-[N'-(3-methyl-2-hydroxybutyryl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
15	8-109	3-[N'-(3-nitrophenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(<i>tert</i> -butylcarbonylmethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
20	8-110	3-[N'-(4-methoxyphenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(2-(N,N-diethylamino)ethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
	8-111	3-[N'-(2-thienylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(2-(N,N-diethylamino)ethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
25	8-112	3-[N'-(3,5-difluorophenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(2-(N,N-diethylamino)ethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
30	8-113	3-[N'-(3-bromophenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(2-(N,N-diethylamino)ethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
35	8-114	3-[N'-(2-phenylthioacetyl)-L-alaninyl]amino-2,3-dihydro-1-(2-(N,N-diethylamino)ethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
40	8-117	3-[N'-(2-cyclohexylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(2-(N,N-diethylamino)ethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
	8-118	3-[N'-(2,3,4,5,6-pentafluorophenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(2-(N,N-diethylamino)ethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
45	8-119	3-[N'-(2-thionaphth-3-ylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(2-(N,N-diethylamino)ethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one

	8-120	3-[N'-(2-phenyl-2-oxoacetyl)-L-alaninyl]amino-2,3-dihydro-1-(2-(N,N-diethylamino)ethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
5	8-123	3-[N'-((3,4-difluorophenyl)acetyl)-L-alaninyl]amino-2,3-dihydro-1-(2-(N,N-diethylamino)ethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
10	8-124	3-[N'-((4-(thien-2-yl)butyryl)-L-alaninyl]amino-2,3-dihydro-1-(2-(N,N-diethylamino)ethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
15	8-125	3-[N'-(5-methylhexanoyl)-L-alaninyl]amino-2,3-dihydro-1-(2-(N,N-diethylamino)ethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
20	8-130	3-[N'-(4-fluorophenyl- α -hydroxyacetyl)-L-alaninyl]amino-2,3-dihydro-1-(2-(N,N-diethylamino)ethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
	8-131	3-[N'-(2,5-difluorophenyl- α -hydroxyacetyl)-L-alaninyl]amino-2,3-dihydro-1-(2-(N,N-diethylamino)ethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
25	8-135	3-[N'-(4,4,4-trifluorobutyryl)-L-alaninyl]amino-2,3-dihydro-1-(2-(N,N-diethylamino)ethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
30	8-136	3-[N'-(4- <i>iso</i> -propylphenylacetyl)-L-alaninyl]amino-2,3-dihydro-1-(2-(N,N-diethylamino)ethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
35	8-137	3-[N'-(3-phenyl-2-hydroxypropionyl)-L-alaninyl]amino-2,3-dihydro-1-(2-(N,N-diethylamino)ethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
40	8-138	3-[N'-(phenyl- α -hydroxyacetyl)-L-alaninyl]amino-2,3-dihydro-1-(2-(N,N-diethylamino)ethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one
45	8-139	3-[N'-(4-chlorophenyl- α -hydroxyacetyl)-L-alaninyl]amino-2,3-dihydro-1-(2-(N,N-diethylamino)ethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one

Example 8-140

Synthesis of

3-[N'-(3,5-Difluorophenyl- α -hydroxyacetyl)-
L-3-thienylglyciny]amino-2,4-dioxo-
1,5-bis(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-
1H-1,5-benzodiazepine

Following General Procedure D above using 3,5-difluoromandelic acid (Fluorochem) and 3-(L-3-thienylglyciny]amino-2,4-dioxo-1,5-bis(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine (Example 8-AB), the title compound was prepared as a solid. The product was purified by LC 2000 chromatography, eluting with hexanes/ethyl acetate (1:1).

Isomer 1:

Melting Point: 191-192°C.

Optical Rotation: $[\alpha] = +21.47 @ 589; +52.17 @ 365$ (c 1, MeOH).

$C_{33}H_{38}F_2N_4O_5S$ (MW = 640); mass spectroscopy found (M+H) 639.1; 640.1.

Anal. calcd for $C_{33}H_{38}F_2N_4O_5S$: C, 61.68; H, 5.89; N, 8.74. Found: C, 61.87; H, 6.08; N, 8.84.

Isomer 2:

Melting Point: 230-231°C.

Optical Rotation: $[\alpha] = +59.26 @ 589; +200.0 @ 365$ (c 1, MeOH).

$C_{33}H_{38}F_2N_4O_5S$ (MW = 640); mass spectroscopy found (M+H) 639.4; 640.4.

Anal. calcd for $C_{33}H_{38}F_2N_4O_5S$: C, 61.68; H, 5.89; N, 8.74. Found: C, 62.01; H, 6.07; N, 8.52.

Example 8-141

Synthesis of

3-[N'-(3,5-Difluorophenyl- α -hydroxyacetyl)-L-alaniny]amino-
2,4-dioxo-1-phenyl-5-methyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine

Following General Procedure D above using 3,5-difluoromandelic acid (Fluorochem) and 3-(L-alaniny]amino-2,4-dioxo-1-phenyl-5-methyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine (Example 8-N), the title compound was

prepared as a solid. The product was purified by LC 2000 chromatography, eluting with hexanes/ethyl acetate (30:70).

Isomer 1:

Melting Point: 212-213°C.

5 Optical Rotation: $[\alpha] = +101.34 @ 589; +491.4 @ 365$ (c 1, MeOH).

$C_{27}H_{24}F_2N_4O_5$ (MW = 522.17); mass spectroscopy found (M+H) 523.3; 521.3.

Isomer 2:

Melting Point: 282-283°C.

10 $C_{27}H_{24}F_2N_4O_5$ (MW = 522.1793); exact mass spectroscopy found (M+) 523.1800.

Isomer 3:

Melting Point: 147-148°C.

15 $C_{27}H_{24}F_2N_4O_5$ (MW = 522.1793); exact mass spectroscopy found (M+) 523.1793.

Isomer 4:

Melting Point: 255-256°C.

$C_{27}H_{24}F_2N_4O_5$ (MW = 522.17); mass spectroscopy found (M+) 523.2.

20 Anal. calcd for $C_{27}H_{24}F_2N_4O_5$: C, 62.07; H, 4.63; N, 10.72. Found: C, 62.18; H, 4.84; N, 10.74.

Example 8-142

Synthesis of

25 3-[N'-(3,5-Difluorophenyl- α -hydroxyacetyl)-L-alaninyl]amino-2-oxo-1-methyl-5-phenyl-1,3,4,5-tetrahydro-1H-1,5-benzodiazepine

Following General Procedure D above using 3,5-difluoromandelic acid (Fluorochem) and 3-(L-alaninyl)amino-2-oxo-1-methyl-5-phenyl-1,3,4,5-tetrahydro-1H-1,5-benzodiazepine (Example 8-M), the title compound was prepared as a solid. The product was purified by LC 2000 chromatography, eluting with hexanes/ethyl acetate (40:60).

30

Isomer 1:

Melting Point: 258-259°C.

C₂₇H₂₆F₂N₄O₄ (MW = 508); mass spectroscopy found (M+H) 507; 508.

Anal. calcd for $C_{27}H_{26}F_2N_4O_4$: C, 63.77; H, 5.16; N, 11.02. Found: C, 63.84; H, 5.34; N, 10.96.

Isomer 2:

5 $C_{27}H_{26}F_2N_4O_4$ (MW = 508); mass spectroscopy found (M+H) 507; 508.

Anal. calcd for $C_{27}H_{26}F_2N_4O_4$: C, 63.77; H, 5.16; N, 11.02. Found: C, 63.74; H, 5.38; N, 10.76.

Isomer 3:

Melting Point: 121-123°C.

10 $C_{27}H_{26}F_2N_4O_4$ (MW = 508); mass spectroscopy found (M+H) 507; 508.

Anal. calcd for $C_{27}H_{26}F_2N_4O_4$: C, 63.77; H, 5.16; N, 11.02. Found: C, 63.55; H, 5.30; N, 10.74.

Isomer 4:

Melting Point: 204-205°C.

15 $C_{27}H_{26}F_2N_4O_4$ (MW = 508); mass spectroscopy found (M+H) 507; 508.

Anal. calcd for $C_{27}H_{26}F_2N_4O_4$: C, 63.77; H, 5.16; N, 11.02. Found: C, 63.23; H, 5.24; N, 10.74.

Example 8-143

20

Synthesis of
3-[N'-(3,5-Difluorophenylacetyl)-L-alaninyl]amino-
L-1H-imidazole[1,2-a]-6-phenyl-1,4-benzodiazepine

25 Following General Procedure D above using 3,5-difluorophenylacetic acid (Oakwood Products, Inc.) and 3-(L-alaninyl)amino-L-1H-imidazole[1,2-a]-6-phenyl-1,4-benzodiazepine (prepared by the methods described in Bock et al., *Bioorganic and Medicinal Chemistry*, Vol. 2, 987-988 (1994); *J. Med. Chem.*, 1988, 31, 176-181; and *J. Org. Chem.*, 1987, 52, 3232), the title compound was prepared as a solid. The product was purified by LC 2000 chromatography, eluting with methanol/dichloromethane (5:95).

30 Isomer 1:

Melting Point: 205-206°C.

Optical Rotation: $[\alpha] = -12.86 @ 589; -135.05 @ 365$ (c 1, MeOH).

$C_{28}H_{23}F_2N_5O_2$ (MW = 499); mass spectroscopy found (M+H) 499.1.

Anal. calcd for $C_{28}H_{23}F_2N_5O_2$: C, 67.33; H, 4.64; N, 14.02. Found: C, 67.49; H, 4.61; N, 13.77.

Isomer 2:

5 Melting Point: 151-153°C.

Optical Rotation: $[\alpha] = -37.41 @ 589; -114.71 @ 365$ (c 1, MeOH).

$C_{28}H_{23}F_2N_5O_2$ (MW = 499.1894); exact mass spectroscopy found (M+H) 499.1898.

10 Anal. calcd for $C_{28}H_{23}F_2N_5O_2$: C, 67.33; H, 4.64; N, 14.02. Found: C, 63.43; H, 4.36; N, 13.10.

Example 8-144

Synthesis of

15 4-[N'-(3,5-Difluorophenylacetyl)-L-alaninyl]amino-L-1H-imidazole[1,2-a]-2,4-dihydro-6-phenyl-1,4-benzodiazepine

Following General Procedure D above using 3,5-difluorophenylacetic acid (Oakwood Products, Inc.) and 3-(L-alaninyl)amino-L-1H-imidazole[1,2-a]-2,4-dihydro-6-phenyl-1,4-benzodiazepine (prepared by the methods described in Bock et al., *Bioorganic and Medicinal Chemistry*, Vol. 2, 987-988 (1994); *J. Med. Chem.*, 1988, 31, 176-181; and *J. Org. Chem.*, 1987, 52, 3232), the title compound was prepared as a solid. The product was purified by LC 2000 chromatography, eluting with methanol/dichloromethane (5:95).

Isomer 1:

Melting Point: 135-136°C.

25 Optical Rotation: $[\alpha] = +15.63 @ 589; -162.5 @ 365$ (c 1, MeOH).

$C_{28}H_{25}F_2N_5O_2$ (MW = 501.2); mass spectroscopy found (M+H) 501.1.

Anal. calcd for $C_{28}H_{25}F_2N_5O_2$: C, 67.06; H, 5.02; N, 13.96. Found: C, 62.9; H, 4.93; N, 12.53.

Isomer 2:

30 Melting Point: 162-165°C.

Optical Rotation: $[\alpha] = -28.66 @ 589; -76.43 @ 365$ (c 1, MeOH).

$C_{28}H_{25}F_2N_5O_2$ (MW = 502.2050); exact mass spectroscopy found (M+H) 502.2050.

Anal. calcd for $C_{28}H_{25}F_2N_5O_2$: C, 67.06; H, 5.02; N, 13.96. Found: C, 62.70; H, 4.78; N, 12.69.

Example 8-145

Synthesis of
4-[N'-(3,5-Difluorophenylacetyl)-L-alaninyl]amino-
L-4H[1,2,4]triazole[4,3-a]-6-phenyl-1,4-benzodiazepine

Following General Procedure D above using 3,5-difluorophenylacetic acid (Oakwood Products, Inc.) and 3-(L-alaninyl)amino-L-4H[1,2,4]triazole[4,3-a]-6-phenyl-1,4-benzodiazepine (prepared by the methods described in Bock et al., *Bioorganic and Medicinal Chemistry*, Vol. 2, 987-988 (1994); *J. Med. Chem.*, 1988, 31, 176-181; and *J. Org. Chem.*, 1987, 52, 3232), the title compound was prepared as a solid (m.p. = 165-167°C). The product was purified by LC 2000 chromatography, eluting with methanol/dichloromethane (4:96).

Optical Rotation: $[\alpha] = -34.63 @ 589; -138.53 @ 365$ (c 1, MeOH).

$C_{27}H_{22}F_2N_6O_2$ (MW = 500); mass spectroscopy found (M+H) 500.1.

Anal. calcd for $C_{27}H_{22}F_2N_6O_2$: C, 64.79; H, 4.43; N, 16.79. Found: C, 63.01; H, 4.73; N, 15.32.

Example 8-146

Synthesis of
3-[N'-(3,5-Difluorophenylacetyl)-L-alaninyl]amino-2,4-dioxo-
1,5-bis-(1-methylethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine

Following General Procedure I above using N-(3,5-difluorophenylacetyl)-L-alanine (Example B) and 3-amino-2,4-dioxo-1,5-bis-(1-methylethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine (Example 8-P), the title compound was prepared as a white solid (melting point = 232-233°C). Purification was by flash chromatography eluting with EtOAc/hexanes (4:1 gradient to 6:1). $R_f = 0.31$ (4:1 EtOAc/hexanes).

$C_{26}H_{30}F_2N_4O_4$ (MW 500.55); mass spectroscopy (MH+) 500.2

Anal. Calcd. for $C_{26}H_{30}F_2N_4O_4$: C, 62.39; H, 6.04; N, 11.19. Found: C, 62.62; H, 6.00; N, 11.21.

Example 8-147

5

Synthesis of
3-[N'-(3,5-Difluorophenylacetyl)-(R)-2-thienylglyciny]amino-
2,4-dioxo-1,5-bis-(1-methylethyl)-
2,3,4,5-tetrahydro-1H-1,5-benzodiazepine

Following General Procedure I above using 3,5-difluorophenylacetic acid
10 (Lancaster) and 3-(R-2-thienylglyciny)-amino-2,4-dioxo-1,5-bis-(1-methylethyl)-
2,3,4,5-tetrahydro-1H-1,5-benzodiazepine hydrochloride (Example 8-Q), the
title compound was prepared as an amorphous white solid. Purification was by
flash chromatography eluting with CH_2Cl_2 /EtOAc (5:1 gradient to 4:1). R_f =
0.34 (4:1 CH_2Cl_2 /EtOAc).

15

$C_{29}H_{30}F_2N_4O_4S$ (MW 568.65); mass spectroscopy (MH+) 568.

Anal. Calcd. for $C_{29}H_{30}F_2N_4O_4S$: C, 61.25; H, 5.32; N, 9.85. Found: C,
61.00; H, 5.42; N, 9.68.

Example 8-148

20

Synthesis of
3-[N'-(Cyclopropylacetyl)-R-2-thienylglyciny]amino-
2,4-dioxo-1,5-bis-(1-methylethyl)-2,3,4,5-
tetrahydro-1H-1,5-benzodiazepine

Following General Procedure I above using cyclopropylacetic acid
25 (Lancaster) and the product from Example 8-Q, the title compound was
prepared as an amorphous white solid. Purification was by flash
chromatography eluting with CH_2Cl_2 /EtOAc (4:1 gradient to 5:2). R_f = 0.26
(4:1 CH_2Cl_2 /EtOAc).

$C_{26}H_{32}N_4O_4S$ (MW 496.63); mass spectroscopy (MH+) 496.5

30

Anal. Calcd. for $C_{26}H_{32}N_4O_4S$: C, 62.88; H, 6.49; N, 11.28. Found: C,
62.65; H, 6.57; N, 11.55.

Example 8-149

Synthesis of
3-[N'-(Cyclopentylacetyl)-R-2-thienylglyciny]amino-
2,4-dioxo-1,5-bis-(1-methylethyl)-2,3,4,5-
tetrahydro-1H-1,5-benzodiazepine

Following General Procedure I above using cyclopentylacetic acid (Aldrich) and the product from Example 8-Q, the title compound was prepared as an amorphous white solid. Purification was by flash chromatography eluting with $\text{CH}_2\text{Cl}_2/\text{EtOAc}$ (5:1 gradient to 4:1). $R_f = 0.26$ (4:1 $\text{CH}_2\text{Cl}_2/\text{EtOAc}$).

$\text{C}_{28}\text{H}_{36}\text{N}_4\text{O}_4\text{S}$ (MW 524.69); mass spectroscopy (MH+) 524.5

Anal. Calcd. for $\text{C}_{28}\text{H}_{36}\text{N}_4\text{O}_4\text{S}$: C, 64.10; H, 6.92; N, 10.68. Found: C, 64.07; H, 6.91; N, 10.67.

Example 8-150

Synthesis of
3-[N'-(3,5-Difluorophenylacetyl)-L-alaniny]amino-
2,4-dioxo-1,5-bis-methyl-2,3,4,5-tetrahydro-
1H-1,5-benzodiazepine

Following General Procedure I above using 3,5-difluorophenylacetic acid (Lancaster) and 3-(L-alaniny)-amino-2,4-dioxo-1,5-bis-methyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine hydrochloride (Example 8-R), the title compound was prepared as a white solid (melting point = 206-207°C). Purification was by flash chromatography eluting with straight EtOAc gradient to EtOAc/Acetone (95:5). $R_f = 0.32$ (EtOAc).

$\text{C}_{22}\text{H}_{22}\text{F}_2\text{N}_4\text{O}_4$ (MW 444.42); mass spectroscopy (MH+) 444.

Anal. Calcd. for $\text{C}_{22}\text{H}_{22}\text{F}_2\text{N}_4\text{O}_4$: C, 59.46; H, 4.99; N, 12.61. Found: C, 59.54; H, 5.09; N, 12.56.

Example 8-151

Synthesis of
3-[N'-(3,5-Difluorophenyl- α -hydroxyacetyl)-L-alaniny]amino-
2,4-dioxo-1,5-bis-methyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine

Following General Procedure I above using 3,5-difluoromandelic acid (Lancaster) and the product from Example 8-R, the title compound was

prepared as an amorphous white solid. Purification was by L.C. 2000 eluting with straight EtOAc then flash chromatography eluting with $\text{CH}_2\text{Cl}_2/\text{Acetone}$ (4:1 gradient to 3:1). $R_f = 0.39$ and 0.34 (EtOAc).

$C_{22}H_{22}F_2N_4O_5$ (MW 460.44); mass spectroscopy (MH+) 461.0.

5 Anal. Calcd. for $C_{22}H_{22}F_2N_4O_3$: C, 57.39; H, 4.82; N, 12.17. Found: C, 57.16; H, 4.88; N, 11.97.

Example 8-152

Synthesis of
3-[N'-(3,5-Difluorophenylacetyl)-L-alaninyl]amino-
2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-
tetrahydro-1H-1,5-benzodiazepine

Following General Procedure I above using 3,5-difluorophenylacetic acid (Lancaster) and 3-(L-alaninyl)amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine hydrochloride (Example 8-S), the title compound was prepared as a white solid (melting point = 197-198°C). Purification was by flash chromatography eluting with CH₂Cl₂/EtOAc (2:1 gradient to 3:4). R_f = 0.23 (CH₂Cl₂/EtOAc, 1:1).

$C_{28}H_{34}F_2N_4O_4$ (MW 528.60); mass spectroscopy (MH+) 528.

20 Anal. Calcd. for $C_{28}H_{34}F_2N_4O_4$: C, 63.62; H, 6.48; N, 10.60. Found: C, 63.75; H, 6.63; N, 10.67.

Example 8-153

25 **Synthesis of**
3-[N'-(Cyclopentylacetyl)-L-alaninyl]amino-2,4-dioxo-
1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine

Following General Procedure I above using cyclopentylacetic acid (Aldrich) and 3-(L-alaninyl)amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine hydrochloride (Example 8-S), the title compound was prepared as an amorphous white solid. Purification was by flash chromatography eluting with CH₂Cl₂/EtOAc (1:1). R_f = 0.31 (CH₂Cl₂/EtOAc, 1:1).

$C_{27}H_{40}N_4O_4$ (MW 484.64); mass spectroscopy (MH+) 484.

Anal. Calcd. for $C_{27}H_{40}N_4O_4$: C, 66.92; H, 8.32; N, 11.56. Found: C, 66.86; H, 8.64; N, 11.41.

Example 8-154

5

Synthesis of
3-[N'-(Cyclopropylacetyl)-L-alaninyl]-amino-2,4-dioxo-
1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine

Following General Procedure I above using cyclopropylacetic acid (Lancaster) and 3-(L-alaninyl)amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine hydrochloride (Example 8-S), the title compound was prepared as a white solid (melting point = 190-191°C). Purification was by flash chromatography eluting with CH_2Cl_2 /EtOAc (1:1 gradient to 3:4) and a second flash chromatography eluting with EtOAc/Toluene (7:3). R_f = 0.28 (EtOAc/Toluene, 7:3).

15

$C_{25}H_{36}N_4O_4$ (MW 456.59); mass spectroscopy (MH⁺) 456.1.

Anal. Calcd. for $C_{25}H_{36}N_4O_4$: C, 65.77; H, 7.95; N, 12.27. Found: C, 66.01; H, 8.03; N, 12.35.

Example 8-155

20

Synthesis of
3-[N'-(3,5-Difluorophenylacetyl)-S-phenylglycinyl]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-
2,3,4,5-tetrahydro-1H-1,5-benzodiazepine

Following General Procedure I above using 3,5-difluorophenylacetic acid (Lancaster) and 3-(S-phenylglycinyl)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine hydrochloride (Example 8-T), the title compound was prepared as a white solid (melting point = 186-187°C). Purification was by flash chromatography eluting with CH_2Cl_2 /EtOAc (7:1 gradient to 4:1). R_f = 0.39 (CH_2Cl_2 /EtOAc, 7:1).

30

$C_{33}H_{36}F_2N_4O_4$ (MW 590.68); mass spectroscopy (MH⁺) 590.0.

Anal. Calcd. for $C_{33}H_{36}F_2N_4O_4$: C, 67.10; H, 6.14; N, 9.49. Found: C, 67.36; H, 6.38; N, 9.56.

Example 8-156

Synthesis of
3-[N'-(3,5-Difluorophenylacetyl)-L-alaninyl]-amino-
2,4-dioxo-1,5-bis-(cyclopropylmethyl)-
2,3,4,5-tetrahydro-1H-1,5-benzodiazepine

Following General Procedure I above using 3,5-difluorophenylacetic acid (Lancaster) and 3-(L-alaninyl)-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine hydrochloride (Example 8-U), the title compound was prepared as a white solid (melting point = 211-212°C). Purification was by flash chromatography eluting with CH₂Cl₂/EtOAc (1:1 gradient to 2:3). R_f = 0.44 (CH₂Cl₂/EtOAc, 1:1).

C₂₈H₃₀F₂N₄O₄ (MW 524.57); mass spectroscopy (MH⁺) 524.1.

Anal. Calcd. for C₂₈H₃₀F₂N₄O₄ : C, 64.11; H, 5.76; N, 10.68. Found: C, 64.07; H, 5.79; N, 10.49.

Example 8-157

Synthesis of
3-[N'-(Cyclopentylacetyl)-L-alaninyl]-amino-
2,4-dioxo-1,5-bis-(cyclopropylmethyl)-
2,3,4,5-tetrahydro-1H-1,5-benzodiazepine

Following General Procedure I above using cyclopentylacetic acid (Aldrich) and 3-(L-alaninyl)-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine hydrochloride (Example 8-U), the title compound was prepared as a white foam. Purification was by flash chromatography eluting with CH₂Cl₂/EtOAc (1:1 gradient to 2:3). R_f = 0.50 (CH₂Cl₂/EtOAc, 1:1).

C₂₇H₃₆N₄O₄ (MW 480.61); mass spectroscopy (MH⁺) 481.2 and (MH⁻) 479.2.

Anal. Calcd. for C₂₇H₃₆N₄O₄: C, 67.48; H, 7.55; N, 11.66. Found: C, 67.33; H, 7.57; N, 11.37.

Example 8-158

Synthesis of
3-[N'-(Cyclopentyl- α -hydroxyacetyl)-L-alaninyl]-amino-
2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-
tetrahydro-1H-1,5-benzodiazepine

Following General Procedure I above using cyclopentyl- α -hydroxyacetic acid (Example P) and 3-(L-alaninyl)-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine hydrochloride (Example 8-U), the title compound was prepared as a white foam. Purification was by L.C. 2000 eluting with CH₂Cl₂/EtOAc (1:1 gradient to 1:2) then flash chromatography eluting with 2:1 EtOAc/CH₂Cl₂. R_f = 0.47 and 0.37 (CH₂Cl₂/EtOAc, 1:2).

C₂₇H₃₆N₄O₅ (MW 496.61); mass spectroscopy (MH⁺) 497.2 and (MH⁻) 495.2

Anal. Calcd. for C₂₇H₃₆N₄O₅ : C, 65.30; H, 7.31; N, 11.28. Found: C, 65.01; H, 7.35; N, 11.28.

Example 8-159

Synthesis of
3-[N'-(3,5-Difluorophenylacetyl)-L-alaninyl]-amino-
2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-
tetrahydro-1H-1,5-benzodiazepine

Following General Procedure I above using 3,5-difluorophenylacetic acid (Lancaster) and 3-(L-alaninyl)-amino-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine hydrochloride (Example 8-V), the title compound was prepared as a white solid (melting point = 194-195°C). Purification was by flash chromatography eluting with CH₂Cl₂/EtOAc (2:1 gradient to 3:2). R_f = 0.46 (CH₂Cl₂/EtOAc, 2:1).

C₃₀H₃₈F₂N₄O₄ (MW 556.66); mass spectroscopy (MH⁺) 557.0 (MH⁻) 555.4.

Anal. Calcd. for C₃₀H₃₈F₂N₄O₄ : C, 64.73; H, 6.88; N, 10.06. Found: C, 64.45; H, 6.82; N, 10.08.

Example 8-160

Synthesis of
3-[N'-(3,5-Difluorophenyl- α -hydroxyacetyl)-L-alaninyl]-amino-
2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-
tetrahydro-1H-1,5-benzodiazepine

5 Following General Procedure I above using 3,5-difluoromandelic acid (Lancaster) and 3-(L-alaninyl)-amino-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine hydrochloride (Example 8-V), the title compound was prepared as a white solid (melting point = 116-126°C).
10 Purification was by flash chromatography eluting with CH₂Cl₂/EtOAc (1:1 gradient to 2:3). R_f = 0.54 and 0.40 (CH₂Cl₂/EtOAc, 1:1).

C₃₀H₃₈F₂N₄O₅ (MW 572.66); mass spectroscopy (MH⁺) 573.4 (MH⁻) 571.6.

15 Anal. Calcd. for C₃₀H₃₈F₂N₄O₅ : C, 62.92; H, 6.69; N, 9.78. Found: C, 62.86; H, 6.54; N, 9.65.

Example 8-161

Synthesis of
3-[N'-(Cyclopentylacetyl)-L-alaninyl]amino-2,4-dioxo-
1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-
tetrahydro-1H-1,5-benzodiazepine

20 Following General Procedure I above using cyclopentylacetic acid (Aldrich) and 3-(L-alaninyl)-amino-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine hydrochloride (Example 8-V), the title
25 compound was prepared as a white amorphous solid. Purification was by flash chromatography eluting with CH₂Cl₂/EtOAc (2:1 gradient to 3:2). R_f = 0.29 (CH₂Cl₂/EtOAc, 2:1).

C₂₉H₄₄N₄O₄ (MW 512.70); mass spectroscopy (MH⁺) 513.6 (MH⁻) 511.6.

30 Anal. Calcd. for C₂₉H₄₄N₄O₄ : C, 67.94; H, 8.65; N, 10.93. Found: C, 68.18; H, 8.60; N, 10.68.

Example 8-162

Synthesis of
3-[N'-(Cyclopentyl- α -hydroxyacetyl)-L-alaninyl]amino-2,4-dioxo-
1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-
tetrahydro-1H-1,5-benzodiazepine

Following General Procedure I above using cyclopentyl- α -hydroxyacetic acid (Example P) and 3-(L-alaninyl)-amino-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine hydrochloride (Example 8-V), the title compound was prepared as a white solid (melting point = 119-129°C). Purification was by flash chromatography eluting with CH₂Cl₂/EtOAc (1:1 gradient to 2:3). R_f = 0.42 and 0.28 (CH₂Cl₂/EtOAc, 1:1).

C₂₉H₄₄N₄O₅ (MW 528.70); mass spectroscopy (MH⁺) 529.2 (MH⁻) 527.4.

Anal. Calcd. for C₂₉H₄₄N₄O₅: C, 65.88; H, 8.39; N, 10.60. Found: C, 65.56; H, 8.03; N, 10.35.

Example 8-163

Synthesis of
3-[N'-(3,5-Difluorophenylacetyl)-L-alaninyl]-amino-2,4-dioxo-
1,5-bis-phenyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine

Following General Procedure I above using 3,5-difluorophenylacetic acid (Lancaster) and 3-(L-alaninyl)-amino-2,4-dioxo-1,5-bis-phenyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine hydrochloride (Example 8-W), the title compound was prepared as a white solid (melting point = 139-141°C).

Purification was by flash chromatography eluting with CH₂Cl₂/EtOAc (1:1). R_f = 0.46 (CH₂Cl₂/EtOAc, 1:1).

C₃₂H₂₆F₂N₄O₄ (MW 568.59); mass spectroscopy (MH⁺) 569.2 (MH⁻) 567.4.

Anal. Calcd. for C₃₂H₂₆F₂N₄O₄: C, 67.60; H, 4.61; N, 9.85. Found: C, 67.39; H, 4.66; N, 9.60.

Example 8-164

Synthesis of
3-[N'-(Cyclopentylacetyl)-L-alaninyl]amino-2,4-dioxo-
1,5-bis-phenyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine

5 Following General Procedure I above using cyclopentylacetic acid (Aldrich) and 3-(L-alaninyl)-amino-2,4-dioxo-1,5-bis-phenyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine hydrochloride (Example 8-W), the title compound was prepared as an amorphous white solid. Purification was by flash chromatography eluting with CH₂Cl₂/EtOAc (1:1). R_f = 0.44 (CH₂Cl₂/EtOAc, 1:1).

10 C₃₁H₃₂N₄O₄ (MW 524.63); mass spectroscopy (MH⁺) 525.2 (MH⁻) 523.2.

Anal. Calcd. for C₃₁H₃₂N₄O₄ : C, 70.97; H, 6.15; N, 10.68. Found: C, 70.67; H, 5.98; N, 10.43.

Example 8-165

15 Synthesis of
3-[N'-(Cyclopentyl- α -hydroxyacetyl)-L-alaninyl]-amino-
2,4-dioxo-1,5-bis-phenyl-2,3,4,5-
tetrahydro-1H-1,5-benzodiazepine

20 Following General Procedure I above using cyclopentyl- α -hydroxyacetic acid (Example P) and 3-(L-alaninyl)-amino-2,4-dioxo-1,5-bis-phenyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine hydrochloride (Example 8-W), the title compound was prepared as a white solid (melting point = 139-149°C).

Purification was by flash chromatography eluting with CH₂Cl₂/EtOAc (1:2). R_f = 0.50 and 0.39 (CH₂Cl₂/EtOAc, 1:2).

25 C₃₁H₃₂N₄O₅ (MW 540.63); mass spectroscopy (MH⁺) 541.2 (MH⁻) 539.6.

Anal. Calcd. for C₃₁H₃₂N₄O₅: C, 68.87; H, 5.97; N, 10.36. Found: C, 68.87; H, 5.88; N, 10.15.

Example 8-166

30 Synthesis of
3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-
2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one

Following General Procedure A above using N-(3,5-difluorophenylacetyl)-L-alanine (Example B) and 3-amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-

benzodiazepin-2-one (prepared as described in Bock M. G.; DiPardo, R. M.; Evans, B. E.; Rittle, K. E.; Veber, D. F.; Freidinger, R. M.; Hirshfield, J.; Springer, J. P. *J. Org. Chem.* **1987**, *52*, 3232), the title compound was prepared as a solid having a melting point of 152-160°C. The reaction was monitored by tlc on silica gel ($R_f = 0.15$ in 50% ethyl acetate/hexanes) and purification was by silica gel chromatography.

NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 7.70$ (t, $J=7.2, 7.2$, 1H); 7.4 (m, 9H); 6.83 (d, $J=5.5$, 2H); 6.7 (m, 1H); 6.50 (d, $J=7.1$, 1H); 5.44 (dd, 2.8, 4.9, 2.8, 1H); 4.7 (m, 1H); 3.53 (s, 2H); 3.45 (s, 3H); 1.46 (dd, $J=4.4, 2.2, 4.9$, 3H).

^{13}C -nmr (CDCl_3): $\delta = 172.9, 167.8, 138.3, 133.4, 127.7, 126.5, 126.3, 125.4, 123.9, 120.3, 117.2, 108.1, 107.8, 98.4, 63.0, 44.7, 40.1, 38.4, 30.9, 14.5, 14.1$.

$\text{C}_{27}\text{H}_{24}\text{F}_2\text{N}_4\text{O}_3$ (MW = 490); mass spectroscopy (MH^+) 491.

The title compound was resolved using a Daicel chiral column (2 x 25 cm, ID x L) (normal phase polysaccharide type; 10 micro particle size). Using a gradient of 40% isopropanol/hexanes (4 mL/min flow rate for 35 minutes), followed by 20% isopropanol/hexanes (3 mL/min), isomer 1 and isomer 2 had retention times of 27.5 and 36.4 minutes, respectively.

Example 8-167

Synthesis of

3-(N'-(3,5-Difluorophenyl- α -hydroxyacetyl)-L-alaninyl)amino-5H-pyrrolo[1,2-a][1,5]benzodiazepin-6(7H)-one

5H-Pyrrolo[1,2-a][1,5]benzodiazepin-6(7H)-one (CAS No. 63743-03-3) was methylated using General Procedure 8-I, aminated by azide transfer using General Procedure 8-D and azide reduction using General Procedure 8-F, and coupled to L-Boc-alanine (Sigma) using General Procedure D. The Boc group was then removed using General Procedure 8-N and the diastereomers were separated by LC chromatography. Each isomer was separately coupled with

(S)-(+)-3,5-difluoromandelic acid (Example L) using General Procedure D to give the title compound.

Isomer 1:

Melting point = 239-240°C.

5 MW = 469.1687; exact mass spectroscopy (M^+) 469.1693.

Optical rotation: $[\alpha] = -121.18^\circ @ 589$ and $-540.33^\circ @ 365$ ($c = 1$, MeOH).

Isomer 2:

Melting point = 144-145°C.

10 MW = 469.1687; exact mass spectroscopy (M^+) 469.1687.

Optical rotation: $[\alpha] = +64.66^\circ @ 589$ and $+255.03^\circ @ 365$ ($c = 1$, MeOH).

15 Using the following combinatorial procedures, the following additional intermediates and examples were prepared.

GENERAL PROCEDURE C-A

To a 4 mL vial containing 60-100 mg (0.06-0.1 mmol) of polymer bound 1-(1-pyrrolidiny)l propyl)-3-ethyl carbodiimide was added 2 mL of a 0.015 mM
20 stock solution of starting material 1 in DMF/chloroform and 1 mL of a 0.0148 mM stock solution of starting material 2 in chloroform. The resulting slurry were shaken for 48 h and filtered. The filtered resin was washed with chloroform and the filtrate was concentrated to dryness under vacuum. All product structures and purities were confirmed by HPLC using UV detection
25 and IEX MS. Samples were submitted for testing with out any further purification.

GENERAL PROCEDURE C-B

To a 4 mL vial was added 840 uL of 0.05 mM stock solution of starting
30 material 1 in DMF/chloroform, 100 uL of a 0.21 mM stock solution of starting material 2 in chloroform and 100 uL of a 0.63 mM stock solution of 1-(3-

dimethylaminopropyl)-3-ethyl carbodiimide in chloroform. After allowing to stand undisturbed for 48 h, the reaction mixture was concentrated and the residue redissolved in 2 mL of a 10% methanol/methylene chloride solution. This solution was then filtered through a pre-washed (methanol) 500 mg SCX column (Varian Sample Preparation; Harbor City California) using an additional 8 mL of the same solvent. The filtrate was concentrated under reduced pressure and the residue was dissolved in 20% methanol/methylene chloride and passed through a plug of silica gel (100 mg, Varian Sample Preparation). The collected filtrate was concentrated under reduced pressure and the crude products were submitted for testing without further purification. Product structure and purity were confirmed by HPLC and IEX MS.

GENERAL PROCEDURE C-C

To a 4 mL vial was added 540 uL of 0.05 mM stock solution of starting material 1 in DMF/chloroform, 100 uL of a 0.44 mM stock solution of starting material 2 in chloroform and 100 uL of a 0.38 mM stock solution of 1-(3-dimethylaminopropyl)-3-ethyl carbodiimide in chloroform. After standing undisturbed for 48 h, the reaction mixture was concentrated and the residue redissolved in 2 mL of a 10% methanol/methylene chloride solution. This solution was then filtered through a pre-washed (methanol) 500 mg SCX column using an additional 8 mL of the same solvent. The filtrate was concentrated under reduced pressure and the residue was dissolved in 20% methanol/methylene chloride and passed through a plug of silica gel (100 mg, Varian Sample Preparation). The collected filtrate was concentrated under reduced pressure and the crude products were submitted for testing without further purification. Product structure and purity were confirmed by HPLC and IEX MS.

GENERAL PROCEDURE C-D

To a 4 mL vial was added 540 uL of 0.05 mM stock solution of starting material 1 in DMF / chloroform, 100 uL of a 0.44 mM stock solution of

starting material 2 in chloroform, 100 uL of a 0.38 mM stock solution of 1-(3-dimethylaminopropyl)-3-ethyl carbodiimide in chloroform and 100 uL of a 0.38 mM stock solution of PP-HOBt in DMF. After standing undisturbed for 48 h, the reaction mixture was concentrated and the residue redissolved in 2 mL of a 10% methanol/methylene chloride solution. This solution was then filtered through a pre-washed (methanol) 500 mg SCX column using an additional 8 mL of the same solvent. The filtrate was concentrated under reduced pressure and the residue was dissolved in 20% methanol/methylene chloride and passed through a plug of silica gel (100 mg, Varian Sample Preparation). The collected filtrate was concentrated under reduced pressure and the crude products were submitted for testing without further purification. Product structure and purity were confirmed by HPLC and IEX MS.

GENERAL PROCEDURE C-E

To a 4 mL vial was added 870 uL of 0.05 mM stock solution of starting material 1 in DMF/chloroform, 1000 uL of a 0.05 mM stock solution of starting material 2 in chloroform, 1000 uL of a 0.05 mM stock solution of 1-(3-dimethylaminopropyl)-3-ethyl carbodiimide in chloroform and 100 uL of a 0.48 mM stock solution of HOBt in DMF. After standing undisturbed for 48 h, the reaction mixture was concentrated and the residue redissolved in 2 mL of a 10% methanol/methylene chloride solution. This solution was then filtered through a pre-washed (methanol) 500 mg SCX column using an additional 8 mL of the same solvent. The filtrate was concentrated under a stream of nitrogen to approximately 1/3 its original volume and then passed over a plug (200 mg) of AG 1-8x anion exchange resin (BioRad; Hercules, California; Columns were pre-washed with 1N NaOH, water and methanol) using an additional 6 mL of 10% methanol/methylene chloride solution. The resulting filtrate was concentrated under vacuum and the crude products were submitted for testing without further purification. Product structure and purity were confirmed by HPLC and IEX MS.

GENERAL PROCEDURE C-F

Starting material 1 (9.1 μ L, 0.109 mmol) was added neat to a mixture of starting material 2 (22.5 mg, 0.054 mmol) and piperidinylmethyl polystyrene (45 mg, 3.6 mmol/g (Fluka)) in 1 mL of methylene. The mixture was shaken
5 for 80 h at ambient temperatures and then treated with methylisocyanate polystyrene (100 mg, 1.0 mmol/g (Novabiochem)) for 24 h with shaking. The reaction mixture was filtered and the resin washed with methylene chloride. The crude product was loaded onto a 500 mg SCX ion exchange column (Varian Sample Preparation), washed 3X with 3 mL of methanol and then
10 eluted with 4 mL of 2 M ammonia methanol. Further purification of the final product was achieved using semi-preparative HPLC (0-100% acetonitrile (0.08 % TFA)/water (0.1 % TFA); 25 mL/min.; 20X50 ODS-A column) to give 17 mg of the final product as an off white foam.

NMR data was as follows:

15 ^1H NMR (300 MHz, CDCl_3) δ 1.45-1.65 (m, 3 H), 1.70-2.00 (m, 4 H), 2.55-2.80 (m, 4 H), 3.25 (s, 2 H), 3.50 (s, 3H), 4.65-4.80 (m, 1 H), 5.45-5.55 (m, 1 H), 7.20-7.80 (m, 11 H).

GENERAL PROCEDURE C-G

20 To a 4 mL vial containing 0.03 mmol of starting material 2 was added 100 μ L of 0.25 mM stock solution of starting material 1 in chloroform, 100 μ L of a 0.3 mM stock solution of 1-(3-dimethylaminopropyl)-3-ethyl carbodiimide in chloroform and 100 μ L of a 0.3 mM stock solution of HOBt in DMF. After standing undisturbed for 48 h, the reaction mixture was concentrated and the
25 residue redissolved in 2 mL of a 10% methanol/methylene chloride solution. This solution was then filtered through a pre-washed (methanol) 500 mg SCX column using an additional 8 mL of the same solvent. The filtrate was concentrated under a stream of nitrogen to approximately 1/3 its original volume and then passed over a plug (200 mg) of AG 1-8x anion exchange resin
30 (BioRad; Hercules, California; Columns were pre-washed with 1N NaOH, water and methanol) using an additional 6 mL of 10% methanol/methylene

chloride solution. The resulting filtrate was concentrated under vacuum and the crude products were submitted for testing without further purification. Product structure and purity were confirmed by HPLC and IEX MS.

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GENERAL PROCEDURE C-H

The intermediates shown in Table C-1 (i.e., Starting material 2) were synthesized in parallel in using the following procedure:

10 Step A: To a solution of 3-(tert-butoxycarbonyl)amino-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one (CA No. 125:33692: 100 mg, 0.28 mmol) in 1 mL of anhydrous DMF was added 600 uL of a solution of 0.5 M potassium bis(trimethylsilyl)amide (0.30 mmol) in toluene. Neat alkyl halide (0.56 mmol; as indicated in Table C-1) was added immediately in one portion and the reaction mixture was left undisturbed overnight. When an alkyl chloride was used, 1 equivalent of sodium iodide was added to the reaction mixture. After concentration under reduced pressure, the crude reaction residue was partitioned between methylene chloride (2 mL) and aqueous saturated bicarbonate (2 mL) and then passed through a 5 g Extralut QE cartridge (EM Science; Gibbstown, NJ) using 10 mL of methylene chloride. The resulting filtrate was concentrated under reduced pressure and the crude product was further purified using automated semi-preparative HPLC (YMC 20 X 50 mm Silica column; gradient elution; 0-5 % (5.5 min.), 5-20 % (3.5 min.), 20-100 % (2 min.), 100% (4 min.) ethyl acetate/methylene chloride, flow rate of 25 mL/min.). Product provided the expected M+1 peak by IEX MS and were carried on without further purification and characterization.

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Step B: The product obtained from Step A was dissolved in 5 mL of a 15 % TFA/methylene chloride solution and allowed to stand undisturbed for 16 h. After concentration under reduced pressure, the TFA salt was dissolved in methanol and loaded directly onto a 1 g SCX column. The column was washed 3 X with 2 mL portions of methanol and the product was eluted from the column using 6 mL of 2.0 M solution of ammonia/methanol. After

30

concentration under reduced pressure, the product were characterized by IEX MS and carried on without further purification.

5 Step C: To the crude product obtained from Step B (1.05 equiv.) was added sequentially a 0.3 mM stock solution of HOBt•H₂O (1.05 equiv.) in DMF, a 0.3 mM stock solution of N-t-BOC-L-alanine (1.0 equiv.) in THF and 0.3 mM stock solution of 1-(3-dimethylaminopropyl)-3-ethyl carbodiimide (1.05 equiv.) in THF. After standing undisturbed for 24 h, the reaction mixture was concentrated and the residue redissolved in 2 mL of a 10% methanol/methylene chloride solution. This solution was then filtered through a pre-washed
10 (methanol) 1 g SCX (Varian Sample Preparation) column using an additional 8 mL of the same solvent. For Example C-V a 1 g Si column (Varian Sample Preparation) was used). The filtrate was concentrated under a stream of nitrogen to approximately 1/3 its original volume and then passed over a plug
15 (500 mg) of AG 1-8x anion exchange resin (BioRad; Hercules, California; Columns were pre-washed with 1N NaOH, water and methanol) using an additional 10 mL of methanol. The resulting filtrate was concentrated under reduced pressure and the crude product was carried on without further purification after characterization by IEX MS.

20 Step D: The crude product obtained from Step C was dissolved in 5 mL of a 15 % TFA/methylene chloride solution and allowed to stand undisturbed for 16 h. After concentration under reduced pressure, the TFA salt was dissolved in methanol and loaded directly onto a 1 g SCX column. The column was
25 washed 3 X with 2 mL portions of methanol and the product were eluted from the column using 6 mL of 2.0 M solution of ammonia/methanol. After concentration under reduced pressure, the product were characterized by IEX MS and carried on without further purification. The intermediates prepared by this method are shown in Table C-A.

TABLE C-A
Intermediates

Ex.	Alkyl Halide	Intermediate	MS
C-A	3-Fluorobenzyl bromide (Aldrich)	3-(L-alaninyl)amino-5-phenyl- 2,3-dihydro-1-(3-fluorobenzyl)- 1H-1,4-benzodiazepin-2-one	431.1
C-B	Benzyl bromide (Aldrich)	3-(L-alaninyl)amino-5-phenyl- 2,3-dihydro-1-(benzyl)-1H-1,4- benzodiazepin-2-one	513.2
C-C	<i>tert</i> -Butylbenzyl bromide (Aldrich)	3-(L-alaninyl)amino-5-phenyl- 2,3-dihydro-1-(4- <i>tert</i> - butylbenzyl)-1H-1,4- benzodiazepin-2-one	469.2
C-D	2-Bromoethylcyclohexane (Fairfield)	3-(L-alaninyl)amino-5-phenyl- 2,3-dihydro-1-(2- cyclohexylethyl)-1H-1,4- benzodiazepin-2-one	433.2
C-E	1-Bromo-3,3-dimethylbutane (Wiley)	3-(L-alaninyl)amino-5-phenyl- 2,3-dihydro-1-(3,3- dimethylbutyl)-1H-1,4- benzodiazepin-2-one	407.2
C-F	Methyl alpha- bromophenylacetate (Aldrich)	3-(L-alaninyl)amino-5-phenyl- 2,3-dihydro-1-(1- methoxycarbonyl-1- phenylmethyl)-1H-1,4- benzodiazepin-2-one	471.2
C-G	1-bromo-2-ethylbutane (Aldrich)	3-(L-alaninyl)amino-5-phenyl- 2,3-dihydro-1-(2-ethylbutyl)-1H- 1,4-benzodiazepin-2-one	407.2
C-H	Bromomethylcyclohexane (Aldrich)	3-(L-alaninyl)amino-5-phenyl- 2,3-dihydro-1- (cyclohexylmethyl)-1H-1,4- benzodiazepin-2-one	419.2
C-I	2-(Bromoethyl)benzene (Aldrich)	3-(L-alaninyl)amino-5-phenyl- 2,3-dihydro-1-(2-phenylethyl)- 1H-1,4-benzodiazepin-2-one	427.2
C-J	3-(Bromopropyl)benzene (K and K Laboratories)	3-(L-alaninyl)amino-5-phenyl- 2,3-dihydro-1-(3-phenylpropyl)- 1H-1,4-benzodiazepin-2-one	441.2

Ex.	Alkyl Halide	Intermediate	MS
C-K	N-(2-Bromoethyl)phthalimide (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-(N-phthalimidyl)ethyl)-1H-1,4-benzodiazepin-2-one	496.2
C-L	2-Phenylbenzyl bromide (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-biphenylmethyl)-1H-1,4-benzodiazepin-2-one	489.2
C-M	Tetrahydrofurfuryl bromide (Lancaster)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-((2-tetrahydrofuranyl)methyl)-1H-1,4-benzodiazepin-2-one	407.2
C-N	2-Bromomethyl-1,4-benzodioxane (Acros)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-(1,4-benzodioxanyl)methyl)-1H-1,4-benzodiazepin-2-one	471.2
C-O	3-Bromomethyl-5-chlorobenzo[b]thiophene (Maybridge)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-((3-(5-chlorobenzo[b] thienyl))methyl)-1H-1,4-benzodiazepin-2-one	503.1
C-P	1-Bromopinacolone (Lancaster)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3,3-dimethyl-2-oxo-propyl)-1H-1,4-benzodiazepin-2-one	421.1
C-Q	5-(Bromomethyl)benzofurazan (Maybridge)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(5-benzofurazanylmethyl)-1H-1,4-benzodiazepin-2-one	455.2
C-R	3-Phenoxypropyl bromide (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3-phenoxypropyl)-1H-1,4-benzodiazepin-2-one	457.2
C-S	6-(Bromomethyl)-2-(trifluoromethyl)quinoline (Maybridge)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(6-(2-trifluoromethylquinolinyl)methyl)-1H-1,4-benzodiazepin-2-one	533.2
C-T	1-bromo-2-methylbutane (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-methylbutyl)-1H-1,4-benzodiazepin-2-one	393.2
C-U	Ethyl bromide (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(ethyl)-1H-1,4-benzodiazepin-2-one	351.2

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Ex.	Alkyl Halide	Intermediate	MS
C-V	3-Picolyl chloride hydrochloride (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3-pyridylmethyl)-1H-1,4-benzodiazepin-2-one	414.1
C-W	1-(2-Chloroacetyl)indoline (Maybridge)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-oxo-2-(N-indolinyl)ethyl)-1H-1,4-benzodiazepin-2-one	482.2
C-Y	4-(Chloromethyl)-3,5-dimethylisoxazole (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-((4-(3,5-dimethyl)isoxazolyl)methyl)-1H-1,4-benzodiazepin-2-one.	432.2
C-Z	2-Bromoethyl methyl ether (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-methoxyethyl)-1H-1,4-benzodiazepin-2-one	381.2

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GENERAL PROCEDURE C-I

To a 4 mL vial containing 0.03 mmol of starting material 2 (from General Procedure C-H) was added 100 uL of 0.25 mM stock solution of starting material 1 in chloroform, 100 uL of a 0.3 mM stock solution of 1-(3-dimethylaminopropyl)-3-ethyl carbodiimide in chloroform and 100 uL of a 0.3 mM stock solution of HOBt in DMF. After standing undisturbed for 48 h, the reaction mixture was concentrated and the residue redissolved in 2 mL of a 10% methanol/methylene chloride solution. This solution was then filtered through a pre-washed (methanol) 500 mg Si column using an additional 8 mL of the same solvent. The filtrate was concentrated under a stream of nitrogen to approximately 1/3 its original volume and then passed over a plug (200 mg) of AG 1-8x anion exchange resin (Columns were pre-washed with 1N NaOH, water and methanol) using an additional 6 mL of 10% methanol/methylene chloride solution. The resulting filtrate was concentrated under vacuum and the crude products were submitted for testing without further purification. Product structure and purity were confirmed by HPLC and IEX MS.

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Example C-AA

Synthesis of
(S)-3-(L-phenylglyciny)amino-
2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one

5 Step A: Synthesis of (S)-3-(N'-(*tert*-Butoxycarbonyl)-L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one

To a solution of triethyl amine (519 uL, 3.8 mmol) and (S)-3-amino-5-phenyl-2-oxo-1,4-benzodiazepine (1.0 g, 3.8 mmol) (prepared according to the
10 procedure of M. G. Bock et al., *J. Org. Chem.* 1987, 52, 3232-3239) in 100 mL of anhydrous methylene chloride at -20°C was added N-Boc-L-phenylglycine fluoride (Carpino et al, *J. Org. Chem.* 1991, 56, 2611-2614) in one portion. The reaction mixture was stirred for 15 min. and quenched with saturated aqueous bicarbonate (10 mL). The layers were separated, the organic
15 layer washed sequentially with saturated aqueous bicarbonate, water and brine and then dried over sodium sulfate. Purification of the crude product using silica gel chromatography (10-50% ethyl acetate / hexane) gave 1.3 g (69%) of a hygroscopic white foam.

NMR data was as follows:

20 ¹H NMR (300 MHz, CDCl₃): δ = 1.35 (br s, 9H), 3.41 (s, 3H), 5.30-5.45 (m, 2H), 5.75-5.95 (m, 1H), 7.15-7.75 (m, 15H).

IR (CDCl₃): 1709.7, 1676.6, 1489, 1166.3 cm⁻¹.

IEX MS (M+1): 498.0.

25 Step B: Synthesis of (S)-3-(L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one

(S)-3-(N'-(*tert*-Butoxycarbonyl)-L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (1.27 g, 2.55 mmol) was added to
30 50 mL of a stirring solution of 15 % TFA in methylene chloride in one portion. After stirring 1 h, the reaction mixture was concentrated under reduced pressure and the residue dissolved in 100 mL of methylene chloride. This solution was washed twice with saturated sodium bicarbonate, once with brine

and then dried over sodium sulfate. Purification of the crude product using silica gel column chromatography (5-10% methanol/methylene chloride) gave 743 mg (73%) of a very light green foam.

NMR data was as follows:

5 ^1H NMR (CDCl_3): δ = 2.05 (br s, 1 H), 3.45 (s, 3 H), 5.51 (d, J = 8.39 Hz, 1H), 7.15-7.70 (m, 14 H), 8.60 (d, J = 830 Hz, 1 H).

IR (CDCl_3): 1673.3, 1601.1, 1506.1 cm^{-1} .

IEX MS ($M+1$): 399.2.

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Example C-AB

Synthesis of 3-(L-Alaninyl)amino-2,3-dihydro-1- (2-oxo-2-phenylethyl)-5-phenyl-1H-1,4-benzodiazepin-2-one

15 Step A: Synthesis of 3-(Benzoxycarbonyl)amino-2,3-dihydro-1-(2-oxo-2-phenylethyl)-5-phenyl-1H-1,4-benzodiazepin-2-one

To a solution of 3-(Benzoxycarbonyl)amino-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one (Bock, M. G. et al, *Tetrahedron Lett.* 1987, 28, 939; 4.0 g, 10.4 mmol) in 40 mL of anhydrous DMF at 0°C was added potassium *tert*-butoxide (1.51 g, 13.5 mmol) in one portion. The reaction mixture was stirred 20 min. and α -bromoacetophenone (Lancaster; Windham, NH; 2.9 g, 14.6 mmol) was added. The reaction mixture was warmed to room temperature over 30 min. and then diluted with 100 mL of water and 200 mL of methylene chloride. The layers were separated. The organic layer was extracted with 25 water and dried over sodium sulfate. Purification of the crude product by silica gel column chromatography (0-5% ethyl acetate/methylene chloride) gave 4.2 g (81%) of an off white foam.

NMR data was as follows:

30 ^1H NMR (300 MHz, CDCl_3): δ = 5.16 (s, 2 H), 5.34 (s, 2 H), 5.50 (d, J = 8.33 Hz, 1 H), 6.70 (d, J = 8.28 Hz, 1 H), 7.20-7.70 (m, 12 H), 7.91 (d, J = 7.54 Hz, 2 H).

IR (CHCl_3): 1706.04, 1685.3, 1505.9, 1489.1, 1450.3, 1244.7 cm^{-1} .

IEX MS ($M+1$): 504.3.

Step B:

Synthesis of 3-Amino-2,3-dihydro-1-(2-oxo-2-phenylethyl)-5-phenyl-1H-1,4-benzodiazepin-2-one

A solution of 3-(Benzyloxycarbonyl)amino-2,3-dihydro-1-(2-oxo-2-phenylethyl)-5-phenyl-1H-1,4-benzodiazepin-2-one (3.7 g, 7.36 mmol) in 100 mL of anhydrous methylene chloride was cooled to 0°C under nitrogen. A stream of anhydrous HBr gas was then bubbled through this solution for 1 h. The bubbler was removed and the reaction was warmed to room temperature under nitrogen. After stirring 1 h the reaction was concentrated under vacuum and the residue was redissolved in 20 mL of methylene chloride. The crude HBr salt of the product was precipitated from solution using 300 mL of anhydrous ether and collected by filtration as a light yellow solid. After washing with ether, the solid was dissolved in methylene chloride and saturated sodium bicarbonate. The layers were separated and the organic layer was extracted with saturated sodium bicarbonate. The combined aqueous layers were then back extracted twice with methylene chloride. The combined organic layers were extracted once with water and dried over sodium sulfate. After concentration under vacuum, 2.27 g of the product was obtained as an orange foam which was carried on without further purification.

NMR data was as follows:

¹H NMR (300 MHz, CDCl₃): δ = 2.60 (br s, 2 H), 4.72 (s, 1 H), 5.34 (s, 2 H), 7.10-7.70 (m, 12 H), 7.91 (d, J = 7.60 Hz, 2 H).

IEX MS (M+1): 370.2

Step C:

Synthesis of 3-(N'-(*tert*-Butoxycarbonyl)-L-alaninyl)amino-2,3-dihydro-1-(2-oxo-2-phenylethyl)-5-phenyl-1H-1,4-benzodiazepin-2-one

To a solution of HOBt-H₂O (697 mg, 5.16 mmol), N,N-diisopropylethylamine (900 uL, 5.16 mmol) and N-t-BOC-L-alanine (975 mg, 5.16 mmol) in 20 mL of anhydrous THF at 0°C was added 1-(3-dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride (EDCI; 986 mg, 5.16 mmol) in one portion. After stirring 5 min., a solution of 3-amino-2,3-dihydro-1-(2-oxo-2-phenylethyl)-5-phenyl-1H-1,4-benzodiazepin-2-one (2.0 g, 5.43

mmol) in 20 mL of anhydrous THF was added via syringe and the reaction mixture was warmed to room temperature and stirred overnight. The reaction mixture was diluted with 200 mL methylene chloride, extracted sequentially with 10 % citric acid, saturated sodium bicarbonate, water and brine and then dried over sodium sulfate. Purification of the crude product using silica gel chromatography (10%-30% ethyl acetate/methylene chloride) gave 2.59 g (93%) of a white foam.

NMR data was as follows:

^1H NMR (300 MHz, CDCl_3): δ = 1.30-1.60 (m, 12 H), 4.35 (br s, 1 H), 5.00-5.50 (m, 3 H), 5.65-5.70 (m, 1 H), 7.15-7.65 (m, 12 H), 7.70-7.80 (m, 1 H), 7.85-7.95 (m, 1 H).

IR (CHCl_3): 1705.8, 1678.8, 1488.7, 1450.2, 1230.4, 1164.4 cm^{-1} .

IEX MS ($M+1$): 541.2.

Step D: Synthesis of 3-(L-Alaninyl)amino-2,3-dihydro-1-(2-oxo-2-phenylethyl)-5-phenyl-1H-1,4-benzodiazepin-2-one

3-(N'-(*tert*-Butoxycarbonyl)-L-alaninyl)amino-2,3-dihydro-1-(2-oxo-2-phenylethyl)-5-phenyl-1H-1,4-benzodiazepin-2-one (2.5 g, 4.63 mmol) was added to 100 mL of a stirring solution of 15 % TFA/methylene chloride in one portion. After stirring 2 h, the reaction mixture was concentrated under reduced pressure and the residue was dissolved in 150 mL of methylene chloride. This solution was washed twice with saturated sodium bicarbonate, once with brine and then dried over sodium sulfate. Purification of the crude product using silica gel column chromatography (1-10% methanol/methylene chloride) gave 1.91 g (94%) of the title compound as a white foam.

NMR data was as follows:

^1H NMR (300 MHz, CDCl_3): δ = 1.30-1.50 (m, 3 H), 1.80-2.20 (br s, 2 H), 3.55-3.75 (m, 1 H), 5.20-5.45 (m, 2 H), 5.67 (t, J = 7.48 Hz, 1 H), 7.20-7.65 (m, 12 H), 7.90 (d, J = 7.7 Hz, 2 H), 8.80 (dd, J_1 = 25.09 Hz, J_2 = 8.33 Hz, 1 H).

EX MS ($M+1$): 441.2.

Example C-AC

Synthesis of
3-(L-Alaninyl)amino-2,3-dihydro-1-
(4,4,4-trifluorobutyl)-5-phenyl-1H-1,4-benzodiazepin-2-one

5 Step A: Synthesis of 3-(Benzoxycarbonyl)amino-2,3-dihydro-1-
 (4,4,4-trifluorobutyl)-5-phenyl-1H-1,4-benzodiazepin-2-one

To a solution of 3-(benzoxycarbonyl)amino-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one (3.7 g, 9.61 mmol) in 40 mL of anhydrous DMF at 0°C was added potassium *tert*-butoxide (1.6 g, 14.4 mmol) in one portion. The
10 reaction mixture was stirred 20 min. and 4,4,4-trifluoro-1-bromobutane (Lancaster; Windham, NH; 2.6 g, 13.4 mmol) was added. The reaction mixture was warmed to room temperature over 30 min. and then diluted with 100 mL of water and 200 mL of methylene chloride. The layers were separated. The organic layer was extracted with water and dried over sodium
15 sulfate. Purification of the crude product by silica gel column chromatography (0-3 % ethyl acetate / methylene chloride) gave 1.52 g (32 %) of an off white foam.

NMR data was as follows:

¹H NMR (300 MHz, CDCl₃): δ = 1.50-2.10 (m, 4 H), 3.70-3.90 (m, 1
20 H), 4.35-4.55 (m, 1 H), 5.15 (s, 2 H), 5.33 (d, J = 8.47 Hz, 1 H), 6.67 (d, J = 8.40 Hz, 1 H), 7.2-7.70 (m, 14 H).

IR (CHCl₃): 1720.4, 1683.0, 1604.8, 1505.5, 1451.1, 1323.9, 1254.5, 1148.4 cm⁻¹.

IEX MS (M+1): 496.3.

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Step B: Synthesis of 3-Amino-2,3-dihydro-1-(4,4,4-trifluorobutyl)-
 5-phenyl-1H-1,4-benzodiazepin-2-one

A solution of 3-(benzoxycarbonyl)amino-2,3-dihydro-1-(4,4,4-trifluorobutyl)-5-phenyl-1H-1,4-benzodiazepin-2-one (1.42 g, 2.87 mmol) in 50
30 mL of anhydrous methylene chloride was cooled to 0°C under nitrogen. A stream of anhydrous HBr gas was slowly bubbled through the solution for 1 h. The bubbler was removed and the reaction was warmed to room temperature under nitrogen. After stirring for 1 h, the reaction was concentrated under

vacuum and the residue was redissolved in 10 mL of methylene chloride. The crude HBr salt of the product was precipitated from solution using 90 mL of anhydrous ether and collected by filtration. After washing with ether, the HBr salt was dissolved in methylene chloride and saturated sodium bicarbonate.

5 The layers were separated and the organic layer was extracted with saturated sodium bicarbonate. The combined aqueous layers were then back extracted twice with methylene chloride. The combined organic layers were extracted once with water and dried over sodium sulfate. After concentration under vacuum, 1.06 g (100%) of the product was obtained as a white foam which was
10 carried on without further purification.

NMR data was as follows:

¹H NMR (300 MHz, CDCl₃): δ = 1.60-2.10 (m, 4 H), 2.76 (br s, 2 H), 3.75-3.85 (m, 1 H), 4.40-4.60 (m, 2 H), 7.20-7.70 (m, 9 H).

IEX MS (M+1): 362.1.

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Step C: Synthesis of 3-(N'-(*tert*-Butoxycarbonyl)-L-alaninyl)amino-2,3-dihydro-1-(4,4,4-trifluorobutyl)-5-phenyl-1H-1,4-benzodiazepin-2-one

To a solution of HOBt-H₂O (373 mg, 2.76 mmol), N,N-diisopropylethylamine (481 uL, 2.76 mmol) and N-t-BOC-L-alanine (522 mg, 2.76 mmol) in 10 mL of anhydrous THF at 0°C was added 1-(3-dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride (EDCI; 527 mg, 2.76 mmol) in one portion. After stirring 5 min., a solution of 3-amino-2,3-dihydro-1-(4,4,4-trifluorobutyl)-5-phenyl-1H-1,4-benzodiazepin-2-one (1.05 g, 2.91 mmol) in 10 mL of anhydrous THF was added via syringe and the reaction mixture was warmed to room temperature and stirred overnight. The reaction mixture was diluted with 100 mL methylene chloride, extracted sequentially with 10% citric acid, saturated sodium bicarbonate, water and brine and then dried over sodium sulfate. Purification of the crude product using silica gel chromatography (10%-30% ethyl acetate/methylene chloride) gave 1.28 g (83%) of a white foam.
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NMR data was as follows:

¹H NMR (300 MHz, CDCl₃): δ = 1.40-2.10 (m, 16 H), 3.70-3.85 (m, 1 H), 4.30-4.55 (m, 2 H), 5.10 (br s, 1 H), 5.45-5.55 (m, 1 H), 7.25-7.80 (m, 10 H).

IR (CDCl₃): 1676.6, 1605.2, 1488.6, 1450.9, 1393.2, 1338.7, 1324.9, 1253.8, 1150.4 cm⁻¹.

IEX MS (M+1): 533.1.

Step D: Synthesis of 3-(L-Alaninyl)amino-2,3-dihydro-1-(4,4,4-trifluorobutyl)-5-phenyl-1H-1,4-benzodiazepin-2-one

3-(N'-(*tert*-Butoxycarbonyl)-L-alaninyl)amino-2,3-dihydro-1-(4,4,4-trifluorobutyl)-5-phenyl-1H-1,4-benzodiazepin-2-one (1.21 g, 2.27 mmol) was added to 50 mL of a stirring solution of 15 % TFA / methylene chloride in one portion. After stirring 2 h, the reaction mixture was concentrated under reduced pressure and the residue was dissolved in 100 mL of methylene chloride. This solution was washed twice with saturated sodium bicarbonate, once with brine and then dried over sodium sulfate. Purification of the crude product using silica gel column chromatography (1-5% methanol / methylene chloride) gave 670 mg (68%) of a light pink foam.

NMR data was as follows:

¹H NMR (300 MHz, CDCl₃): δ = 1.43 (t, J = 7.0 Hz, 3 H), 1.60-2.20 (m, 7 H), 3.60-3.85 (m, 2 H), 4.35-4.55 (m, 1 H), 5.51 (dd, J₁ = 8.36 Hz, J₂ = 2.48 Hz, 1 H), 7.20-7.70 (m, 9 H), 8.80 (dd, J₁ = 27.73 Hz, J₂ = 8.34 Hz, 1 H).

IEX MS (M+1): 433.2.

Example C-AD

**Synthesis of
3-(N'-(Chloroacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one**

A solution of 3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (20.0 mg, 0.0595 mmol), α-chloroacetyl chloride (5.9 uL, 0.0744 mmol) and piperidinylmethyl polystyrene (59.5 mg, 3.6 mmol/g

(Fluka)) in 1 mL of methylene chloride were shaken for 20 min. Aminomethyl polystyrene (58 mg, 3.0 mmol/g (Advanced Chemtech)) was then added and the reaction mixture was shaken for an additional 15 min. and filtered. Removal of the solvent under reduced pressure provided 23.9 mg (98%) of the crude
5 product which was used without further purification.

NMR data was as follows:

^1H NMR (300 MHz, CDCl_3): δ = 1.40-1.60 (m, 3 H), 3.40-3.6 (m, 3 H), 4.1 (s, 2 H), 4.60-4.80 (m, 1 H), 5.45-5.50 (m, 1 H), 7.20-7.90 (m, 11 H).

10 Using the procedures indicated, the compounds shown in Table C-1 were prepared.

Table C-1

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-1	3-(N'-(3,4-Methylenedioxyphenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3,4-Methylenedioxyphenylacetic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	498.8
8C-2	3-(N'-(2-Methoxyphenoxyacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2-Methoxyphenoxyacetic acid (Lancaster)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	500.8
8C-3	3-(N'-(4-Isopropylphenoxyacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-Isopropylphenoxyacetic acid (Lancaster)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	513.0
8C-4	3-(N'-(Ethoxyacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Ethoxyacetic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	422.6

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-5	3-(N'-(4-Phenoxyphenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-Phenoxyphenylacetic acid (Trans World)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	547.0
8C-6	3-(N'-(4-Ethoxyphenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-Ethoxyphenylacetic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	501.1
8C-7	3-(N'-(2,5-Dimethoxyphenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2,5-Dimethoxyphenylacetic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	514.8
8C-8	3-(N'-(3,5-Difluorobenzoyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3,5-Difluorobenzoic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	476.8
8C-9	3-(N'-(o-Tolylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	o-Tolylacetic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	470.0

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-10	3-(N'-(3,3-Diphenylpropionyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3,3-Diphenylpropionic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	545.0
8C-11	3-(N'-(3-Phenoxypropionyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-Phenoxypropionic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	485.0
8C-12	3-(N'-(Indole-3-acetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Indole-3-acetic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	494.0
8C-13	3-(N'-(4-(Trifluoromethyl)phenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-(Trifluoromethyl)phenylacetic acid (Maybridge)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	523.0
8C-14	3-(N'-(4-Methylphenoxy)acetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	(4-Methylphenoxy)acetic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	485.0

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-16	3-(N'-(4-(Hydroxymethyl)phenoxyacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-(Hydroxymethyl)phenoxyacetic acid (Sigma)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	500.8
8C-17	3-(N'-(2-Phenoxyphenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2-Phenoxyphenylacetic acid (Trans World)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	546.8
8C-18	3-(N'-(3-Phenoxyphenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-Phenoxyphenylacetic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	547.0
8C-19	3-(N'-(3,4-dichlorophenoxyacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3,4-dichlorophenoxyacetic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	539.2
8C-20	3-(N'-(4-Fluorophenoxyacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-Fluorophenoxyacetic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	489.0

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-21	3-(N'-(Methylthio)acetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	(Methylthio)acetic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	424.8
8C-22	3-(N'-(Methoxyacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Methoxyacetic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	409.0
8C-23	(S)-3-(N'-(Phenoxyacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Phenoxyacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	471.0
8C-24	(S)-3-(N'-(Phenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Phenylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	455.0
8C-25	(S)-3-(N'-(2-Phenoxybutyryl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2-Phenoxybutyric acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	498.8

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-26	(S)-3-(N'-(3-Methoxyphenoxycetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-Methoxyphenoxycetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	501.0
8C-28	(S)-3-(N'-(4-Butoxyphenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-Butoxyphenylacetic acid (Lancaster)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	526.8
8C-29	(S)-3-(N'-(3-(2-Methoxyphenyl)propionyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-(2-Methoxyphenyl)propionic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	498.8
8C-30	(S)-3-(N'-(4-Fluorophenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-Fluorophenylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	472.8
8C-31	(S)-3-(N'-(Isopropoxycetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Isopropoxycetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	436.8

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-32	(S)-3-(N'-(1-Phenyl-1H-tetrazole-5-acetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	1-Phenyl-1H-tetrazole-5-acetic acid (Raap, R. Can. J. Chem. 1968, 46(13), 2255-61)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	523.0
8C-33	(S)-3-(N'-(3-(3,4-methylenedioxyphenyl)propionyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-(3,4-methylenedioxyphenyl)propionic acid (Apin)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	513.2
8C-34	(S)-3-(N'-(3-Cyclopentylpropionyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-Cyclopentylpropionic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	461.0
8C-35	(S)-3-(N'-(2-Cyclopentene-1-acetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2-Cyclopentene-1-acetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	445.0
8C-36	(S)-3-(N'-(2-Chloro-6-fluorophenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2-Chloro-6-fluorophenylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	507.0

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-37	(S)-3-(N'-(Cyclohexylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Cyclohexylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	461.0
8C-38	(S)-3-(N'-(2,5-Difluorophenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2,5-Difluorophenylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	491.2
8C-39	(S)-3-(N'-(Pentafluorophenoxyacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Pentafluorophenoxyacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	561.0
8C-40	(S)-3-(N'-(3,5-Dimethylphenoxyacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3,5-Dimethylphenoxyacetic acid (Sigma-Aldrich Rare Chemicals)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	498.8
8C-41	(S)-3-(N'-(4-Chlorophenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-Chlorophenylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	489.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-42	(S)-3-(N'-(3-Chlorophenoxyacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-Chlorophenoxyacetic acid (Lancaster)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	505.0
8C-43	(S)-3-(N'-(Benzo [b] thiophene-3-acetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Benzo [b] thiophene-3-acetic acid (Lancaster)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	511.2
8C-44	(S)-3-(N'-(Benzoylformyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Benzoylformic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	468.8
8C-45	(S)-3-(N'-(3,5-Dimethoxyphenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3,5-Dimethoxyphenylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	515.0
8C-46	(S)-3-(N'-(2,5-Dimethylphenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2,5-Dimethylphenylacetic acid (Lancaster)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	483.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-47	(S)-3-(N'-(2,6-Difluorophenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2,6-Difluorophenylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	491.2
8C-48	(S)-3-(N'-(2,4-Difluorophenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2,4-Difluorophenylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	491.0
8C-49	(S)-3-(N'-(Mesitylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Mesitylacetic acid (Lancaster)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	497.0
8C-50	(S)-3-(N'-(4-Biphenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-Biphenylacetic acid (Lancaster)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	531.2
8C-51	(S)-3-(N'-(3,4-Difluorophenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3,4-Difluorophenylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	491.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-52	(S)-3-(N'-(trans-Styrylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	trans-Styrylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	481.2
8C-53	(S)-3-(N'-(3-Benzoylpropionyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-Benzoylpropionic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	497.0
8C-54	(S)-3-(N'-(trans-3-Hexenoyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	trans-3-Hexenoic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	433.2
8C-55	(S)-3-(N'-(Heptanoyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Heptanoic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	449.0
8C-56	(S)-3-(N'-(3-(4-Methylphenyl)propionyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-(4-Methylphenyl)propionic acid (Lancaster)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	483.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-57	(S)-3-(N'-(3-(4-Chlorophenyl)propionyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-(4-Chlorophenyl)propionic acid (Trans World)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	503.0
8C-58	(S)-3-(N'-(3-Phenylbutyryl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-Phenylbutyric acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	483.2
8C-59	(S)-3-(N'-(4-(4-Methoxyphenyl)butyryl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-(4-Methoxyphenyl)butyric acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	513.2
8C-60	(S)-3-(N'-(3-Methoxycarbonylpropionyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	mono-Methyl succinate (3-Methoxycarbonylpropionic acid) (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	451.0
8C-61	(S)-3-(N'-(4-Phenylbutyryl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-Phenylbutyric acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	483.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-62	(S)-3-(N'-(3-(Benzylthio)propionyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-(Benzylthio)propionic acid (Sigma-Aldrich Rare Chemicals)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	515.2
8C-63	(S)-3-(N'-(3-Methylpentanoyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-Methylpentanoic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	435.2
8C-64	(S)-3-(N'-(6-Methoxycarbonylheptanoyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Suberic acid monomethyl ester(6-Methoxycarbonylheptanoic acid)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	507.0
8C-65	(S)-3-(N'-(2-Indanylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2-Indanylacetic acid (Lancaster)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-B	495.0
8C-66	(S)-3-(N'-(4-Methoxyphenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-Methoxyphenylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	485.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-67	(S)-3-(N'-(o-Chlorophenoxyacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	o-Chlorophenoxyacetic acid (Lancaster)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	505.0
8C-68	(S)-3-(N'-(2-Thiopheneacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2-Thiopheneacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	461.0
8C-69	(S)-3-(N'-(3-(Trifluoromethyl)phenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-(Trifluoromethyl)phenylacetic acid (Marshallton)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	523.0
8C-70	(S)-3-(N'-(p-Tolylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	p-Tolylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	469.0
8C-71	(S)-3-(N'-(2,6-Difluoromandelyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2,6-Difluoromandelic acid (Fluorochem)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-D	448.0

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-72	(S)-3-(N'-(4-Methoxyphenyl)propionyl)-L-alaninylamino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-(4-Methoxyphenyl)propionic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	499.0
8C-73	(S)-3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	491.0
8C-74	(S)-3-(N'-(m-Tolylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	m-Tolylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	469.0
8C-75	(S)-3-(N'-(3-Fluorophenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-Fluorophenylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	473.0
8C-76	(S)-3-(N'-(4-Chlorophenoxyacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-Chlorophenoxyacetic acid (Grand Island Biological Company)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	505.0

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-77	(S)-3-(N'-(2-Naphthylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2-Naphthylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	505.2
8C-78	(S)-3-(N'-(3-Chlorophenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-Chlorophenylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	489.2
8C-79	(S)-3-(N'-(3-Methylphenoxycetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-Methylphenoxycetic acid (Lancaster)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	485.2
8C-80	(S)-3-(N'-(3,4-Methylenedioxyphenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3,4-Methylenedioxyphenylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	499.0
8C-81	(S)-3-(N'-(2-Methoxyphenoxycetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2-Methoxyphenoxycetic acid (Lancaster)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	501.0

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-82	(S)-3-(N'-(4-Isopropylphenoxyacetyl))-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-Isopropylphenoxyacetic acid (Lancaster)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	513.2
8C-83	(S)-3-(N'-(4-Phenoxyphenylacetyl))-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-Phenoxyphenylacetic acid (Trans World)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	547.0
8C-84	(S)-3-(N'-(4-Phenylmercaptoacetyl))-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Phenylmercaptoacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	487.2
8C-85	(S)-3-(N'-(4-Ethoxyphenylacetyl))-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-Ethoxyphenylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	499.0

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-86	(S)-3-(N'-(2,5-Dimethoxyphenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2,5-Dimethoxyphenylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	515.0
8C-87	(S)-3-(N'-(o-Tolylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	o-Tolylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	469.0
8C-88	(S)-3-(N'-(3,3-Diphenylpropionyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3,3-Diphenylpropionic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	545.3
8C-89	(S)-3-(N'-(3-Phenoxypropionyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-Phenoxypropionic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	485.4
8C-90	(S)-3-(N'-(Indole-3-acetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Indole-3-acetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	494.0

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-91	(S)-3-(N'-(4-(Trifluoromethyl)phenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-(Trifluoromethyl)phenylacetic acid (Maybridge)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	523.0
8C-92	(S)-3-(N'-(3,5-Bis(trifluoromethyl)phenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3,5-Bis(trifluoromethyl)phenylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	591.0
8C-93	(S)-3-(N'-(2-Phenoxyphenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2-Phenoxyphenylacetic acid (Trans World)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	547.0
8C-94	(S)-3-(N'-(3-Phenoxyphenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-Phenoxyphenylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-D	547.0

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-95	(S)-3-(N'-(4-Fluorophenoxyacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-Fluorophenoxyacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	489.2
8C-96	(S)-3-(N'-(2,4-Dichlorophenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2,4-Dichlorophenylacetic acid (Fairfield)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	523.0
8C-97	(S)-3-(N'-(Methylthioacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	(Methylthio)acetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	425.0
8C-98	(S)-3-(N'-(4-Fluoromandelyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-Fluoromandelic acid (Lancaster)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-D	489.0
8C-99	(S)-3-(N'-(4-Thionaphthenacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-Thionaphthenacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	511.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-100	(S)-3-(N'-(Methoxyacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Methoxyacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	409.0
8C-101	(S)-3-(N'-(Ethoxyacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Ethoxyacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	422.8
8C-102	(S)-3-(N'-(3-Indolepropionyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-Indolepropionic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	508.2
8C-103	(S)-3-(N'-(3-(2-Chlorophenyl)propionyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-(2-Chlorophenyl)propionic acid (Trans World)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	503.0
8C-104	(S)-3-(N'-(Butyryl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Butyric acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	407.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-105	(S)-3-(N'-(Hexanoyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Hexanoic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	435.0
8C-106	(S)-3-(N'-(5-Phenylpentanoyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	5-Phenylvaleric acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	497.0
8C-107	(S)-3-(N'-(4-(2-Thienyl)butyryl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-(2-Thienyl)butyric acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	489.2
8C-108	(S)-3-(N'-(4-Nitrophenoxyacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-Nitrophenoxyacetic acid (Apin)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	516.2
8C-109	(S)-3-(N'-(3-(3-Methoxyphenyl)propionyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-(3-Methoxyphenyl)propionic acid (Lancaster)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	499.0

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-110	(S)-3-(N'-(5-Methylhexanoyl))-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	5-Methylhexanoic acid (Pfalz and Bauer)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	449.0
8C-111	(S)-3-(N'-(Hydrocinnamyl))-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Hydrocinnamic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	469.0
8C-112	(S)-3-(N'-(Octanoyl))-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Octanoic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	463.2
8C-113	(S)-3-(N'-(3-(3-Hydroxyphenyl)propionyl))-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-(3-Hydroxyphenyl)propionic acid (Lancaster)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-D	485.2
8C-114	(S)-3-(N'-(3-(4-Hydroxyphenyl)propionyl))-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-(4-Hydroxyphenyl)propionic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-D	485.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-115	(S)-3-(N'-(3,4,5-Trifluorophenylacetyl))-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3,4,5-Trifluorophenylacetic acid (Fluorochem)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	509.0
8C-116	(S)-3-(N'-(5-Hydantoinacetyl))-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	5-Hydantoinacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	477.0
8C-117	(S)-3-(N'-(Cyclopentylacetyl))-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	447.0
8C-118	(S)-3-(N'-(3-(Trifluoromethyl)butyryl))-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-(Trifluoromethyl)butyric acid (Fluorochem)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	475.0
8C-119	(S)-3-(N'-(2-Methyl-3-Benzofuranacetyl))-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2-Methyl-3-Benzofuranacetic acid (Maybridge)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	509.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-120	(S)-3-(N'-(Propionyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Propionic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	393.0
8C-121	(S)-3-(N'-(Cyclopropylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Cyclopropylacetic acid (Lancaster)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	419.0
8C-122	(S)-3-(N'-(3-Methoxypropionyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-Methoxypropionic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	423.2
8C-123	(S)-3-(N'-(5-(Thienyl)pentanoyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	5-(Thienyl)pentanoic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	503.0
8C-124	(S)-3-(N'-(3-(4-Fluorophenyl)propionyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-(4-Fluorophenyl)propionic acid (Trans World)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	487.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-125	(S)-3-(N'-(3-(4-Fluorophenoxy)propionyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-(4-Fluorophenoxy)propionic acid (Maybridge)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	503.0
8C-126	(S)-3-(N'-(2-Norbornanecetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2-Norbornanecetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	473.0
8C-128	(S)-3-(N'-(2,3-Difluoromandelyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2,3-Difluoromandelic acid (Fluorochem)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	507.0
8C-129	(S)-3-(N'-(3-Pentenyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-Pentenoic acid (Fluka)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	419.0
8C-130	(S)-3-(N'-(4-(2,4-dichlorophenoxy)butyryl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-(2,4-dichlorophenoxy)butyric acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	567.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-131	(S)-3-(N'-(2,3-Dichlorophenoxyacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2,3-Dichlorophenoxyacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	539.2
8C-133	(S)-3-(N'-(2-Fluorophenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2-Fluorophenylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	473.0
8C-135	(S)-3-(N'-(2-Nitrophenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2-Nitrophenylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	499.8
8C-136	(S)-3-(N'-(4-(Hydroxymethyl)phenoxyacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-(Hydroxymethyl)phenoxyacetic acid (Sigma)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	501.0
8C-137	(S)-3-(N'-(2-Fluoro-3-(trifluoromethyl)phenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2-Fluoro-3-(trifluoromethyl)phenylacetic acid (Fluorochem)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	541.0

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-138	(S)-3-(N'-(2,4,6-Trifluorophenylacetyl))-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2,4,6-Trifluorophenylacetic acid (Fluorochem)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	509.0
8C-139	(S)-3-(N'-(4-Fluoro-2-(trifluoromethyl)phenylacetyl))-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-Fluoro-2-(trifluoromethyl)phenylacetic acid (Fluorochem)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	541.0
8C-140	(S)-3-(N'-(4,4,4-Trifluorobutyl))-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	461.0
8C-141	(S)-3-(N'-(2-Fluoro-4-(trifluoromethyl)phenylacetyl))-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2-Fluoro-4-(trifluoromethyl)phenylacetic acid (Fluorochem)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	541.0
8C-142	(S)-3-(N'-(4-Bromophenylacetyl))-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-Bromophenylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	533.0

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-143	(S)-3-(N'-(3-(4-Fluorobenzoyl)propionyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-(4-Fluorobenzoyl)propionic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	515.0
8C-144	(S)-3-(N'-(2-Methylphenoxy)acetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	(2-Methylphenoxy)acetic acid (Lancaster)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	485.2
8C-145	(S)-3-(N'-(4-Methoxyphenoxy)acetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-Methoxyphenoxyacetic acid (Lancaster)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	501.0
8C-146	(S)-3-(N'-(3-(Phenylsulfonyl)propionyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-(Phenylsulfonyl)propionic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	531 (M-1)

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-147	(S)-3-(N'-(2-Methoxyphenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2-Methoxyphenylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	485.2
8C-148	(S)-3-(N'-(2-Bromophenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2-Bromophenylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	535.0
8C-149	(S)-3-(N'-(p-Isopropyl phenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	p-Isopropyl phenylacetic acid (Lancaster)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	497.0
8C-150	(S)-3-(N'-(4-Pentenoyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-Pentenoyl acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	419.0
8C-151	(S)-3-(N'-(4-Hydroxyphenoxycetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-Hydroxyphenoxycetic acid (Acros)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-D	487.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-152	(S)-3-(N'-(4-Oxopentanoyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Levulinic acid (4-Oxopentanoic acid) (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	433.1 (M-1)
8C-153	(S)-3-(N'-(2-Hydroxyphenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2-Hydroxyphenylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-D	471.0
8C-154	(S)-3-(N'-(3,4-Dimethoxyphenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3,4-Dimethoxyphenylacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	515.0
8C-155	(S)-3-(N'-(3-(4-Methoxybenzoyl)propionyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-(4-Methoxybenzoyl)propionic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	527.0
8C-156	(S)-3-(N'-(Thiophene-3-acetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Thiophene-3-acetic acid (Acros)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	461.0

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-157	(S)-3-(N'-(6-Phenylhexanoyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	6-Phenylhexanoic acid (Avocado)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	511.2
8C-158	(S)-3-(N'-(Isovaleryl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Isovaleric acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	420.8
8C-159	(S)-3-(N'-(2,3,5-Trifluorophenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2,3,5-Trifluorophenylacetic acid (Fluorochem)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	508.8
8C-160	(S)-3-(N'-(2,4,5-Trifluorophenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2,4,5-Trifluorophenylacetic acid (Fluorochem)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	509.0
8C-161	(S)-3-(N'-(1-Adamantanecacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	1-Adamantanecacetic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	513.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-162	(S)-3-(N'-(Cyclohexanepentanoyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Cyclohexanepentanoic acid (Aldrich)	(S)-3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-C	503.0
8C-163	(S)-3-(N'-(2-Thiopheneacetyl)-L-phenylglycinyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2-Thiopheneacetic acid (Aldrich)	(S)-3-(L-phenylglycinyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	523.0
8C-164	(S)-3-(N'-(3-(Trifluoromethyl)phenylacetyl)-L-phenylglycinyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-(Trifluoromethyl)phenylacetic acid (Marshallton)	(S)-3-(L-phenylglycinyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	585.0
8C-165	(S)-3-(N'-(3,5-Difluorophenylacetyl)-L-phenylglycinyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	(S)-3-(L-phenylglycinyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	553.0
8C-166	(S)-3-(N'-(m-Tolylacetyl)-L-phenylglycinyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	m-Tolylacetic acid (Aldrich)	(S)-3-(L-phenylglycinyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	531.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-167	(S)-3-(N'-(3-Fluorophenylacetyl)-L-phenylglycyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-Fluorophenylacetic acid (Aldrich)	(S)-3-(L-phenylglycyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	535.2
8C-168	(S)-3-(N'-(3-Bromophenylacetyl)-L-phenylglycyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-Bromophenylacetic acid (Aldrich)	(S)-3-(L-phenylglycyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	595.2
8C-169	(S)-3-(N'-(3-Chlorophenylacetyl)-L-phenylglycyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-Chlorophenylacetic acid (Aldrich)	(S)-3-(L-phenylglycyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	551.2
8C-170	(S)-3-(N'-(3,4-Methylenedioxyphenylacetyl)-L-phenylglycyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3,4-Methylenedioxyphenylacetic acid (Aldrich)	(S)-3-(L-phenylglycyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	561.2
8C-171	(S)-3-(N'-(Phenylmercaptoacetyl)-L-phenylglycyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Phenylmercaptoacetic acid (Aldrich)	(S)-3-(L-phenylglycyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	549.0

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-173	Bis(trifluoromethyl)phenylacetyl-L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3,5-Bis(trifluoromethyl)phenylacetic acid (Aldrich)	(S)-3-(L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	653.0
8C-174	(S)-3-(N'-(Methylthio)acetyl)-L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	(Methylthio)acetic acid (Aldrich)	(S)-3-(L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	487.2
8C-175	(S)-3-(N'-(Phenoxyacetyl)-L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Phenoxyacetic acid (Aldrich)	(S)-3-(L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	533.0
8C-176	(S)-3-(N'-(Phenylacetyl)-L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Phenylacetic acid (Aldrich)	(S)-3-(L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	517.2
8C-177	(S)-3-(N'-(Cyclohexylacetyl)-L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Cyclohexylacetic acid (Aldrich)	(S)-3-(L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	523.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-178	(S)-3-(N'-(2,5-Difluorophenylacetyl)-L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2,5-Difluorophenylacetic acid (Aldrich)	(S)-3-(L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	553.0
8C-179	(S)-3-(N'-(Benzo [b] thiophene-3-acetyl)-L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Benzo [b] thiophene-3-acetic acid (Aldrich)	(S)-3-(L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	573.2
8C-180	(S)-3-(N'-(benzoylformyl)-L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Benzoylformic acid (Aldrich)	(S)-3-(L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	531.2
8C-181	(S)-3-(N'-(2,6-Difluorophenylacetyl)-L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2,6-Difluorophenylacetic acid (Aldrich)	(S)-3-(L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	553.0
8C-182	(S)-3-(N'-(2,4-Difluorophenylacetyl)-L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2,4-Difluorophenylacetic acid (Aldrich)	(S)-3-(L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	553.0

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-183	(S)-3-(N'-(3,4-Difluorophenylacetyl)-L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3,4-Difluorophenylacetic acid (Aldrich)	(S)-3-(L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	553.0
8C-184	(S)-3-(N'-(Butyryl)-L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Butyric acid (Aldrich)	(S)-3-(L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	469.0
8C-185	(S)-3-(N'-(Heptanoyl)-L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Heptanoic acid (Aldrich)	(S)-3-(L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	511.2
8C-186	(S)-3-(N'-(4-(2-Thienyl)butyryl)-L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-(2-Thienyl)butyric acid (Aldrich)	(S)-3-(L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	551.0
8C-187	(S)-3-(N'-(5-Methylhexanoyl)-L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	5-Methylhexanoic acid (Pfaltz and Bauer)	(S)-3-(L-phenylglyciny)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	511.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-188	(S)-3-(N'-(Hydrocinnamyl))-L-phenylglycylamino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Hydrocinnamic acid (Aldrich)	(S)-3-(L-phenylglycylamino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	531.2
8C-189	(S)-3-(N'-(Cyclopentylacetyl))-L-phenylglycylamino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	(S)-3-(L-phenylglycylamino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	509.2
8C-190	(S)-3-(N'-(Propionyl))-L-phenylglycylamino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Propionic acid (Aldrich)	(S)-3-(L-phenylglycylamino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	455.0
8C-191	(S)-3-(N'-(3,4,5-Trifluorophenylacetyl))-L-phenylglycylamino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3,4,5-Trifluorophenylacetic acid (Fluorochem)	(S)-3-(L-phenylglycylamino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	571.0
8C-192	(S)-3-(N'-(4-Phenylbutyl))-L-phenylglycylamino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-Phenylbutyric acid (Aldrich)	(S)-3-(L-phenylglycylamino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AA)	C-C	545.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-193	3-(N'-(2-Thiopheneacetyl))-L-alaninyl)amino-2,3-dihydro-5-phenyl-1-(4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one	2-Thiopheneacetic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-5-phenyl-1-(4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one (Example C-AC)	C-E	557.2
8C-194	3-(N'-(2-Thiopheneacetyl))-L-alaninyl)amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one	2-Thiopheneacetic acid (Aldrich)	3-(L-alaninyl)amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AB)	C-E	565.2
8C-195	3-(N'-(2-Thiopheneacetyl))-L-alaninyl)amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one	2-Thiopheneacetic acid (Aldrich)	3-(L-alaninyl)amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one (Example C-AH)	C-E	468.1
8C-196	3-(N'-(2-Thiopheneacetyl))-L-alaninyl)amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2-Thiopheneacetic acid (Aldrich)	3-(L-alaninyl)amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-C)	C-E	495.1
8C-197	3-(N'-(2-Thiopheneacetyl))-L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	2-Thiopheneacetic acid (Aldrich)	3-(L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-F)	C-E	529.1 531.1

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-198	3-(N'-(2-Thiopheneacetyl))-L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	2-Thiopheneacetic acid (Aldrich)	3-(L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example C-AI)	C-E	467.1
8C-199	3-(N'-(2-Thiopheneacetyl))-L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	2-Thiopheneacetic acid (Aldrich)	3-(L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-G)	C-E	467.2
8C-200	3-(N'-(2-Thiopheneacetyl))-L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	2-Thiopheneacetic acid (Aldrich)	3-(L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-D)	C-E	557.1 559.1
8C-201	3-(N'-(2-Thiopheneacetyl))-L-alaninyl)amino)-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	2-Thiopheneacetic acid (Aldrich)	3-(L-alaninyl)amino)-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine (Example 8-V)	C-E	527.3

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-202	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-2,3-dihydro-5-phenyl-1-(4,4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-5-phenyl-1-(4,4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one (Example C-AC)	C-E	587.2
8C-203	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AB)	C-E	595.2
8C-204	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one (Example C-AH)	C-E	498.1
8C-205	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-C)	C-E	525.2
8C-206	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-F)	C-E	559.1 561.1

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-207	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example C-AI)	C-E	497.1
8C-208	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-G)	C-E	497.2
8C-209	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-D)	C-E	587.1 590.1
8C-210	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine (Example 8-V)	C-E	557.3

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-211	3-(N'-(3-Fluorophenylacetyl)-L-alaninyl)amino-2,3-dihydro-5-phenyl-1-(4,4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one	3-Fluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-5-phenyl-1-(4,4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one (Example C-AC)	C-E	569.2
8C-212	3-(N'-(3-Fluorophenylacetyl)-L-alaninyl)amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one	3-Fluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AB)	C-E	577.2
8C-213	3-(N'-(3-Fluorophenylacetyl)-L-alaninyl)amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one	3-Fluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one (Example C-AH)	C-E	480.1
8C-214	3-(N'-(3-Fluorophenylacetyl)-L-alaninyl)amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-Fluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-C)	C-E	507.2
8C-215	3-(N'-(3-Fluorophenylacetyl)-L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	3-Fluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-F)	C-E	541.1 543.1

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-216	3-(N'-(3-Fluorophenylacetyl))-L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	3-Fluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example C-AI)	C-E	479.1
8C-217	3-(N'-(3-Fluorophenylacetyl))-L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	3-Fluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-G)	C-E	479.2
8C-218	3-(N'-(3-Fluorophenylacetyl))-L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	3-Fluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-D)	C-E	571.1 573.1
8C-219	3-(N'-(3-Fluorophenylacetyl))-L-alaninyl)amino)-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-Fluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino)-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine (Example 8-V)	C-E	539.3

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-220	3-(N'-(Methylthio)acetyl)-L-alaninyl)amino-2,3-dihydro-5-phenyl-1-(4,4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one	(Methylthio)acetic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-5-phenyl-1-(4,4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one (Example C-AC)	C-E	521.2
8C-221	3-(N'-(Methylthio)acetyl)-L-alaninyl)amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one	(Methylthio)acetic acid (Aldrich)	3-(L-alaninyl)amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AB)	C-E	529.2
8C-222	3-(N'-(Methylthio)acetyl)-L-alaninyl)amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one	(Methylthio)acetic acid (Aldrich)	3-(L-alaninyl)amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one (Example C-AH)	C-E	432.1
8C-223	3-(N'-(Methylthio)acetyl)-L-alaninyl)amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	(Methylthio)acetic acid (Aldrich)	3-(L-alaninyl)amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-C)	C-E	459.1
8C-224	3-(N'-(Methylthio)acetyl)-L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	(Methylthio)acetic acid (Aldrich)	3-(L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-F)	C-E	493.1 495.1

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-225	3-(N'-(Methylthio)acetyl)-L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	(Methylthio)acetic acid (Aldrich)	3-(L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example C-AI)	C-E	431.1
8C-226	3-(N'-(Methylthio)acetyl)-L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	(Methylthio)acetic acid (Aldrich)	3-(L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-G)	C-E	431.2
8C-227	3-(N'-(Methylthio)acetyl)-L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	(Methylthio)acetic acid (Aldrich)	3-(L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-D)	C-E	521.1 523.1
8C-228	3-(N'-(Methylthio)acetyl)-L-alaninyl)-amino-)-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	(Methylthio)acetic acid (Aldrich)	3-(L-alaninyl)-amino-)-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine (Example 8-V)	C-E	491.3

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-229	3-(N'-(Phenylacetyl))-L-alaninyl)amino-2,3-dihydro-5-phenyl-1-(4,4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one	Phenylacetic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-5-phenyl-1-(4,4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one (Example C-AC)	C-E	551.2
8C-230	3-(N'-(Phenylacetyl))-L-alaninyl)amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one	Phenylacetic acid (Aldrich)	3-(L-alaninyl)amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AB)	C-E	559.5
8C-231	3-(N'-(Phenylacetyl))-L-alaninyl)amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one	Phenylacetic acid (Aldrich)	3-(L-alaninyl)amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one (Example C-AH)	C-E	462.2
8C-232	3-(N'-(Phenylacetyl))-L-alaninyl)amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Phenylacetic acid (Aldrich)	3-(L-alaninyl)amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-C)	C-E	489.2
8C-233	3-(N'-(Phenylacetyl))-L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	Phenylacetic acid (Aldrich)	3-(L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-F)	C-E	523.1 525.1

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-234	3-(N'-(Phenylacetyl)-L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	Phenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example C-AI)	C-E	461.1
8C-235	3-(N'-(Phenylacetyl)-L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	Phenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-G)	C-E	461.2
8C-236	3-(N'-(Phenylacetyl)-L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	Phenylacetic acid (Aldrich)	3-(L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-D)	C-E	553.1 554.1
8C-237	3-(N'-(Phenylacetyl)-L-alaninyl)amino-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Phenylacetic acid (Aldrich)	3-(L-alaninyl)amino-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine (Example 8-V)	C-E	521.3

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-238	3-(N'-(Benzoylformyl)-L-alaninyl)amino-2,3-dihydro-5-phenyl-1-(4,4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one	Benzoylformic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-5-phenyl-1-(4,4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one (Example C-AC)	C-E	565.2
8C-239	3-(N'-(Benzoylformyl)-L-alaninyl)amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one	Benzoylformic acid (Aldrich)	3-(L-alaninyl)amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AB)	C-E	573.2
8C-240	3-(N'-(Benzoylformyl)-L-alaninyl)amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one	Benzoylformic acid (Aldrich)	3-(L-alaninyl)amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one (Example C-AH)	C-E	476.1
8C-241	3-(N'-(Benzoylformyl)-L-alaninyl)amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Benzoylformic acid (Aldrich)	3-(L-alaninyl)amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-C)	C-E	503.1
8C-242	3-(N'-(Benzoylformyl)-L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	Benzoylformic acid (Aldrich)	3-(L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-F)	C-E	537.1 539.1

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-243	3-(N'-(Benzoylformyl)-L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	Benzoylformic acid (Aldrich)	3-(L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example C-AI)	C-E	475.1
8C-244	3-(N'-(Benzoylformyl)-L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	Benzoylformic acid (Aldrich)	3-(L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-G)	C-E	475.2
8C-245	3-(N'-(Benzoylformyl)-L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	Benzoylformic acid (Aldrich)	3-(L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-D)	C-E	567.1 568.1
8C-246	3-(N'-(Benzoylformyl)-L-alaninyl)amino-)-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Benzoylformic acid (Aldrich)	3-(L-alaninyl)amino-)-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine (Example 8-V)	C-E	535.3

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-247	3-(N'-(Butyryl)-L-alaninyl)amino-2,3-dihydro-5-phenyl-1-(4,4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one	Butyric acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-5-phenyl-1-(4,4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one (Example C-AC)	C-E	503.2
8C-248	3-(N'-(Butyryl)-L-alaninyl)amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one	Butyric acid (Aldrich)	3-(L-alaninyl)amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AB)	C-E	511.2
8C-249	3-(N'-(Butyryl)-L-alaninyl)amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one	Butyric acid (Aldrich)	3-(L-alaninyl)amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one (Example C-AH)	C-E	414.1
8C-250	3-(N'-(Butyryl)-L-alaninyl)amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Butyric acid (Aldrich)	3-(L-alaninyl)amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-C)	C-E	441.2
8C-251	3-(N'-(Butyryl)-L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	Butyric acid (Aldrich)	3-(L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-F)	C-E	475.1 477.1

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-252	3-(N'-(Butyryl)-L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	Butyric acid (Aldrich)	3-(L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example C-AI)	C-E	413.1
8C-253	3-(N'-(Butyryl)-L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	Butyric acid (Aldrich)	3-(L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-G)	C-E	413.2
8C-254	3-(N'-(Butyryl)-L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	Butyric acid (Aldrich)	3-(L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-D)	C-E	503.1 506.1
8C-255	3-(N'-(Butyryl)-L-alaninyl)amino-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Butyric acid (Aldrich)	3-(L-alaninyl)amino-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine (Example 8-V)	C-E	473.3

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-256	3-(N'-(4-(2-Thienyl)butyl)-L-alaninyl)amino-2,3-dihydro-5-phenyl-1-(4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one	4-(2-Thienyl)butyric acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-5-phenyl-1-(4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one (Example C-AC)	C-E	585.2
8C-257	3-(N'-(4-(2-Thienyl)butyl)-L-alaninyl)amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one	4-(2-Thienyl)butyric acid (Aldrich)	3-(L-alaninyl)amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AB)	C-E	593.2
8C-258	3-(N'-(4-(2-Thienyl)butyl)-L-alaninyl)amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one	4-(2-Thienyl)butyric acid (Aldrich)	3-(L-alaninyl)amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one (Example C-AH)	C-E	496.1
8C-259	3-(N'-(4-(2-Thienyl)butyl)-L-alaninyl)amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-(2-Thienyl)butyric acid (Aldrich)	3-(L-alaninyl)amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-C)	C-E	523.2
8C-260	3-(N'-(4-(2-Thienyl)butyl)-L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	4-(2-Thienyl)butyric acid (Aldrich)	3-(L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-F)	C-E	557.1 559.1

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-261	3-(N'-(4-(2-Thienyl)butyryl)-L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	4-(2-Thienyl)butyric acid (Aldrich)	3-(L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example C-AI)	C-E	495.1
8C-262	3-(N'-(4-(2-Thienyl)butyryl)-L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	4-(2-Thienyl)butyric acid (Aldrich)	3-(L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-G)	C-E	495.2
8C-263	3-(N'-(4-(2-Thienyl)butyryl)-L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	4-(2-Thienyl)butyric acid (Aldrich)	3-(L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-D)	C-E	585.1 587.1
8C-264	3-(N'-(4-(2-Thienyl)butyryl)-L-alaninyl)-amino-)-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4-(2-Thienyl)butyric acid (Aldrich)	3-(L-alaninyl)-amino-)-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine (Example 8-V)	C-E	555.3

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-265	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-2,3-dihydro-5-phenyl-1-(4,4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-5-phenyl-1-(4,4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one (Example C-AC)	C-E	543.3
8C-266	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AB)	C-E	551.3
8C-267	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one (Example C-AH)	C-E	454.2
8C-268	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-C)	C-E	481.2
8C-269	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-F)	C-E	515.2 517.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-270	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example C-AI)	C-E	453.1
8C-271	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-G)	C-E	453.3
8C-272	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-D)	C-E	543.1 546.1
8C-273	3-(N'-(Cyclopentylacetyl)-L-alaninyl)-amino-)-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)-amino-)-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine (Example 8-F)	C-E	513.3

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-274	3-(N'-(3-(Trifluoromethyl)butyl)-L-alaninyl)amino-2,3-dihydro-5-phenyl-1-(4,4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one	3-(Trifluoromethyl)butyric acid (Fluorochem)	3-(L-alaninyl)amino-2,3-dihydro-5-phenyl-1-(4,4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one (Example C-AC)	C-E	571.2
8C-275	3-(N'-(3-(Trifluoromethyl)butyl)-L-alaninyl)amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one	3-(Trifluoromethyl)butyric acid (Fluorochem)	3-(L-alaninyl)amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AB)	C-E	579.2
8C-276	3-(N'-(3-(Trifluoromethyl)butyl)-L-alaninyl)amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one	3-(Trifluoromethyl)butyric acid (Fluorochem)	3-(L-alaninyl)amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one (Example C-AH)	C-E	482.1
8C-277	3-(N'-(3-(Trifluoromethyl)butyl)-L-alaninyl)amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-(Trifluoromethyl)butyric acid (Fluorochem)	3-(L-alaninyl)amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-C)	C-E	509.1

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-278	3-(N'-(3-(Trifluoromethyl)butyl)-L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	3-(Trifluoromethyl)butyric acid (Fluorochem)	3-(L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-F)	C-E	543.1 545.1
8C-279	3-(N'-(3-(Trifluoromethyl)butyl)-L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	3-(Trifluoromethyl)butyric acid (Fluorochem)	3-(L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example C-AI)	C-E	481.1
8C-280	3-(N'-(3-(Trifluoromethyl)butyl)-L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	3-(Trifluoromethyl)butyric acid (Fluorochem)	3-(L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-G)	C-E	481.2
8C-281	3-(N'-(3-(Trifluoromethyl)butyl)-L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	3-(Trifluoromethyl)butyric acid (Fluorochem)	3-(L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-D)	C-E	573.1 574.1

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-282	3-(N'-(3-(Trifluoromethyl)butyl)-L-alaninyl)-amino-2,4-dioxo-1,5-bis-(2,2-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepin-2-one	3-(Trifluoromethyl)butyric acid (Fluorochem)	3-(L-alaninyl)-amino-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine (Example 8-V)	C-E	541.3
8C-283	3-(N'-(4,4,4-Trifluorobutyl)-L-alaninyl)-amino-2,3-dihydro-5-phenyl-1-(4,4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)-amino-2,3-dihydro-5-phenyl-1-(4,4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one (Example C-AC)	C-E	557.2
8C-284	3-(N'-(4,4,4-Trifluorobutyl)-L-alaninyl)-amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)-amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AB)	C-E	565.2
8C-285	3-(N'-(4,4,4-Trifluorobutyl)-L-alaninyl)-amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)-amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one (Example C-AH)	C-E	468.1
8C-286	3-(N'-(4,4,4-Trifluorobutyl)-L-alaninyl)-amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)-amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-C)	C-E	495.1

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-287	3-(N'-(4,4,4-Trifluorobutyl)-L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-F)	C-E	529.1 531.1
8C-288	3-(N'-(4,4,4-Trifluorobutyl)-L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example C-AI)	C-E	467.1
8C-289	3-(N'-(4,4,4-Trifluorobutyl)-L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-G)	C-E	467.2
8C-290	3-(N'-(4,4,4-Trifluorobutyl)-L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-D)	C-E	559.1 560.1

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-291	3-(N'-(4,4,4-Trifluorobutyl)-L-alaninyl)-amino-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)-amino-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine (Example 8-V)	C-E	527.3
8C-292	3-(N'-(Isovaleryl)-L-alaninyl)-amino-2,3-dihydro-5-phenyl-1-(4,4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one	Isovaleric acid (Aldrich)	3-(L-alaninyl)-amino-2,3-dihydro-5-phenyl-1-(4,4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one (Example C-AC)	C-E	517.2
8C-293	3-(N'-(Isovaleryl)-L-alaninyl)-amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one	Isovaleric acid (Aldrich)	3-(L-alaninyl)-amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AB)	C-E	525.3
8C-294	3-(N'-(Isovaleryl)-L-alaninyl)-amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one	Isovaleric acid (Aldrich)	3-(L-alaninyl)-amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one (Example C-AH)	C-E	428.2
8C-295	3-(N'-(Isovaleryl)-L-alaninyl)-amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Isovaleric acid (Aldrich)	3-(L-alaninyl)-amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-C)	C-E	455.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-296	3-(N'-(Isovaleryl)-L-alaninyl)amino-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	Isovaleric acid (Aldrich)	3-(L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-F)	C-E	489.1 491.1
8C-297	3-(N'-(Isovaleryl)-L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	Isovaleric acid (Aldrich)	3-(L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example C-AI)	C-E	427.1
8C-298	3-(N'-(Isovaleryl)-L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	Isovaleric acid (Aldrich)	3-(L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-G)	C-E	427.2
8C-299	3-(N'-(Isovaleryl)-L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	Isovaleric acid (Aldrich)	3-(L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-D)	C-E	519.1 520.1

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-300	3-(N'-(Isovaleryl)-L-alaninyl)-amino-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Isovaleric acid (Aldrich)	3-(L-alaninyl)-amino-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine (Example 8-V)	C-E	487.3
8C-301	3-(N'-(L-alpha-Hydroxyisocaproyl)-L-alaninyl)amino-2,3-dihydro-5-phenyl-1-(4,4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one	L-alpha-Hydroxyisocaproic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-5-phenyl-1-(4,4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one (Example C-AC)	C-E	547.3
8C-302	3-(N'-(L-alpha-Hydroxyisocaproyl)-L-alaninyl)amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one	L-alpha-Hydroxyisocaproic acid (Aldrich)	3-(L-alaninyl)amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AB)	C-E	555.3
8C-303	3-(N'-(L-alpha-Hydroxyisocaproyl)-L-alaninyl)amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one	L-alpha-Hydroxyisocaproic acid (Aldrich)	3-(L-alaninyl)amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one (Example C-AH)	C-E	458.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-304	3-(N'-(L-alpha-Hydroxyisocaproyl)-L-alaninyl)amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	L-alpha-Hydroxyisocaproic acid (Aldrich)	3-(L-alaninyl)amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-C)	C-E	485.2
8C-305	3-(N'-(L-alpha-Hydroxyisocaproyl)-L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	L-alpha-Hydroxyisocaproic acid (Aldrich)	3-(L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-F)	C-E	519.1 521.1
8C-306	3-(N'-(L-alpha-Hydroxyisocaproyl)-L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	L-alpha-Hydroxyisocaproic acid (Aldrich)	3-(L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example C-AI)	C-E	457.1
8C-307	3-(N'-(L-alpha-Hydroxyisocaproyl)-L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	L-alpha-Hydroxyisocaproic acid (Aldrich)	3-(L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-G)	C-E	457.3

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-308	3-(N'-(L-alpha-Hydroxyisocaproyl)-L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	L-alpha-Hydroxyisocaproic acid (Aldrich)	3-(L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-D)	C-E	549.1 550.2
8C-309	3-(N'-(L-alpha-Hydroxyisocaproyl)-L-alaninyl)-amino-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	L-alpha-Hydroxyisocaproic acid (Aldrich)	3-(L-alaninyl)-amino-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine (Example 8-V)	C-E	517.3
8C-310	3-(N'-(L-(+)-Mandelyl)-L-alaninyl)amino-2,3-dihydro-5-phenyl-1-(4,4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one	L-(+)-Mandelic acid (Sigma)	3-(L-alaninyl)amino-2,3-dihydro-5-phenyl-1-(4,4,4-trifluorobutyl)-1H-1,4-benzodiazepin-2-one (Example C-AC)	C-E	567.2
8C-311	3-(N'-(L-(+)-Mandelyl)-L-alaninyl)amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one	L-(+)-Mandelic acid (Sigma)	3-(L-alaninyl)amino-1-(2-oxo-2-phenylethyl)-2,3-dihydro-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AB)	C-E	575.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-312	3-(N'-(L-(+)-Mandelyl)-L-alaninyl)amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one	L-(+)-Mandelic acid (Sigma)	3-(L-alaninyl)amino-1-methyl-2,3-dihydro-5-(2-thiazolyl)-1H-1,4-benzodiazepin-2-one (Example C-AH)	C-E	478.1
8C-313	3-(N'-(L-(+)-Mandelyl)-L-alaninyl)amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	L-(+)-Mandelic acid (Sigma)	3-(L-alaninyl)amino-7-chloro-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-C)	C-E	505.2
8C-314	3-(N'-(L-(+)-Mandelyl)-L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	L-(+)-Mandelic acid (Sigma)	3-(L-alaninyl)amino-7-chloro-5-(2-chlorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-F)	C-E	539.1 541.1
8C-315	3-(N'-(L-(+)-Mandelyl)-L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	L-(+)-Mandelic acid (Sigma)	3-(N'-(L-alaninyl)amino-5-(2-thienyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example C-AI)	C-E	477.1
8C-316	3-(N'-(L-(+)-Mandelyl)-L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	L-(+)-Mandelic acid (Sigma)	3-(L-alaninyl)amino-5-cyclohexyl-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-G)	C-E	477.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-317	3-(N'-(L-(+)-Mandelyl)-L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one	L-(+)-Mandelic acid (Sigma)	3-(L-alaninyl)amino-7-bromo-5-(2-fluorophenyl)-2,3-dihydro-1-methyl-1H-1,4-benzodiazepin-2-one (Example 8-D)	C-E	567.1 569.1
8C-318	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3-fluorobenzyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3-fluorobenzyl)-1H-1,4-benzodiazepin-2-one (Example C-A)	C-G	585.1
8C-319	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(benzyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(benzyl)-1H-1,4-benzodiazepin-2-one (Example C-B)	C-G	567.1
8C-320	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(4-tert-butylbenzyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(4-tert-butylbenzyl)-1H-1,4-benzodiazepin-2-one (Example C-C)	11	623.2
8C-321	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-cyclohexylethyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-cyclohexylethyl)-1H-1,4-benzodiazepin-2-one (Example C-D)	C-G	587.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-322	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3,3-dimethylbutyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3,3-dimethylbutyl)-1H-1,4-benzodiazepin-2-one (Example C-E)	C-G	561.2
8C-323	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(1-methoxycarbonyl-1-phenylmethyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(1-methoxycarbonyl-1-phenylmethyl)-1H-1,4-benzodiazepin-2-one (Example C-F)	C-G	625.1
8C-324	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-ethylbutyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-ethylbutyl)-1H-1,4-benzodiazepin-2-one (Example C-G)	C-G	561.2
8C-325	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(cyclohexylmethyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(cyclohexylmethyl)-1H-1,4-benzodiazepin-2-one (Example C-H)	C-G	573.2
8C-326	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-phenylethyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-phenylethyl)-1H-1,4-benzodiazepin-2-one (Example C-I)	C-G	581.1

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-327	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3-phenylpropyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3-phenylpropyl)-1H-1,4-benzodiazepin-2-one (Example C-I)	C-G	595.2
8C-328	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-(N-phthalimidy)ethyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-(N-phthalimidy)ethyl)-1H-1,4-benzodiazepin-2-one (Example C-K)	C-G	650.1
8C-329	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-biphenylmethyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-biphenylmethyl)-1H-1,4-benzodiazepin-2-one (Example C-L)	C-G	643.2
8C-330	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-tetrahydrofuranymethyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-tetrahydrofuranymethyl)-1H-1,4-benzodiazepin-2-one (Example C-M)	C-G	561.1
8C-331	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-(1,4-benzodioxanylmethyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-(1,4-benzodioxanylmethyl)-1H-1,4-benzodiazepin-2-one (Example C-N)	C-G	625.1

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-332	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3-(5-chlorobenzo[b]thienyl)methyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-((3-(5-chlorobenzo[b]thienyl)methyl)-1H-1,4-benzodiazepin-2-one (Example C-O)	C-G	657.1
8C-333	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3,3-dimethyl-2-oxopropyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3,3-dimethyl-2-oxopropyl)-1H-1,4-benzodiazepin-2-one (Example C-P)	C-G	575.1
8C-334	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(5-benzofurazanylmethyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(5-benzofurazanylmethyl)-1H-1,4-benzodiazepin-2-one (Example C-Q)	C-G	609.1
8C-335	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3-phenoxypropyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3-phenoxypropyl)-1H-1,4-benzodiazepin-2-one (Example C-R)	C-G	611.1

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-336	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(6-(2-trifluoromethylquinolinyl)methyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(6-(2-trifluoromethylquinolinyl)methyl)-1H-1,4-benzodiazepin-2-one (Example C-S)	C-G	686.1
8C-337	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-methylbutyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-methylbutyl)-1H-1,4-benzodiazepin-2-one (Example C-T)	C-G	547.2
8C-338	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(ethyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(ethyl)-1H-1,4-benzodiazepin-2-one (Example C-U)	C-G	505.1
8C-339	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3-pyridylmethyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3-pyridylmethyl)-1H-1,4-benzodiazepin-2-one (Example C-V)	C-I	568.1
8C-340	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-oxo-2-(N-indolinyl)ethyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-oxo-2-(N-indolinyl)ethyl)-1H-1,4-benzodiazepin-2-one (Example C-W)	C-G	676.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-341	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(4-(3,5-dimethylisoxazolyl)methyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(4-(3,5-dimethylisoxazolyl)methyl)-1H-1,4-benzodiazepin-2-one (Example C-Y)	C-G	586.1
8C-342	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-methoxyethyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-methoxyethyl)-1H-1,4-benzodiazepin-2-one (Example C-Z)		
8C-343	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(benzyl)-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(benzyl)-1H-1,4-benzodiazepin-2-one (Example C-B)	C-G	523.2
8C-344	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(4- <i>tert</i> -butylbenzyl)-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(4- <i>tert</i> -butylbenzyl)-1H-1,4-benzodiazepin-2-one (Example C-C)	C-G	579.2
8C-345	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-cyclohexylethyl)-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-cyclohexylethyl)-1H-1,4-benzodiazepin-2-one (Example C-D)	C-G	543.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-346	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3,3-dimethylbutyl)-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3,3-dimethylbutyl)-1H-1,4-benzodiazepin-2-one (Example C-E)	C-G	517.2
8C-347	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(isopropyl)-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(isopropyl)-1H-1,4-benzodiazepin-2-one (Example 8-L)	C-G	475.2
8C-348	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(1-methoxycarbonyl-1-phenylmethyl)-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(1-methoxycarbonyl-1-phenylmethyl)-1H-1,4-benzodiazepin-2-one (Example C-F)	C-G	581.2
8C-349	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-ethylbutyl)-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-ethylbutyl)-1H-1,4-benzodiazepin-2-one (Example C-G)	C-G	517.2
8C-350	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(cyclohexylmethyl)-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(cyclohexylmethyl)-1H-1,4-benzodiazepin-2-one (Example C-H)	C-G	529.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-351	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-phenylethyl)-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-phenylethyl)-1H-1,4-benzodiazepin-2-one (Example C-I)	C-G	537.2
8C-352	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3-phenylpropyl)-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3-phenylpropyl)-1H-1,4-benzodiazepin-2-one (Example C-J)	C-G	551.2
8C-353	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-(N-phthalimidy)ethyl)-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-(N-phthalimidy)ethyl)-1H-1,4-benzodiazepin-2-one (Example C-K)	C-G	606.2
8C-354	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-biphenylmethyl)-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-biphenylmethyl)-1H-1,4-benzodiazepin-2-one (Example C-L)	C-G	599.2
8C-355	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3-(5-chlorobenzo[b]thienyl)methyl)-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3-(5-chlorobenzo[b]thienyl)methyl)-1H-1,4-benzodiazepin-2-one (Example C-O)	C-G	613.1

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-356	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-1H-1,4-benzodiazepin-2-one (Example C-P)	C-G	531.2
8C-357	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(5-benzofurazanylmethyl)-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(5-benzofurazanylmethyl)-1H-1,4-benzodiazepin-2-one (Example C-Q)	C-G	565.2
8C-358	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3-phenoxypropyl)-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3-phenoxypropyl)-1H-1,4-benzodiazepin-2-one (Example C-R)	C-G	567.2
8C-359	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(6-(2-trifluoromethylquinolinyl)methyl)-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(6-(2-trifluoromethylquinolinyl)methyl)-1H-1,4-benzodiazepin-2-one (Example C-S)	C-G	642.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-360	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(cyclopropylmethyl)-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(cyclopropylmethyl)-1H-1,4-benzodiazepin-2-one (Example 8-L)	C-G	487.2
8C-361	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-methylbutyl)-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-methylbutyl)-1H-1,4-benzodiazepin-2-one (Example C-T)	C-G	503.2
8C-362	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(ethyl)-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(ethyl)-1H-1,4-benzodiazepin-2-one (Example C-U)	C-G	461.2
8C-363	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(4-(3,5-dimethylisoxazolyl)methyl)-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(4-(3,5-dimethylisoxazolyl)methyl)-1H-1,4-benzodiazepin-2-one (Example C-Y)	C-G	542.2
8C-364	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(propyl)-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(propyl)-1H-1,4-benzodiazepin-2-one (Example 8-L)	C-G	475.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-365	3-(N'-(Cyclopentylacetyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-methoxyethyl)-1H-1,4-benzodiazepin-2-one	Cyclopentylacetic acid (Aldrich)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(methoxyethyl)-1H-1,4-benzodiazepin-2-one (Example C-Z)	C-G	491.2
8C-366	3-(N'-(4,4,4-Trifluorobutyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(benzyl)-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(benzyl)-1H-1,4-benzodiazepin-2-one (Example C-B)	C-G	537.1
8C-367	3-(N'-(4,4,4-Trifluorobutyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(4-tert-butylbenzyl)-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(4-tert-butylbenzyl)-1H-1,4-benzodiazepin-2-one (Example C-C)	C-G	593.2
8C-368	3-(N'-(4,4,4-Trifluorobutyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-cyclohexylethyl)-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-cyclohexylethyl)-1H-1,4-benzodiazepin-2-one (Example C-D)	C-G	557.2
8C-369	3-(N'-(4,4,4-Trifluorobutyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3,3-dimethylbutyl)-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3,3-dimethylbutyl)-1H-1,4-benzodiazepin-2-one (Example C-E)	C-G	531.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-370	3-(N'-(4,4,4-Trifluorobutyryl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(isopropyl)-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(isopropyl)-1H-1,4-benzodiazepin-2-one (Example 8-L)	C-G	489.1
8C-371	3-(N'-(4,4,4-Trifluorobutyryl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(1-methoxycarbonyl-1-phenylmethyl)-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(1-methoxycarbonyl-1-phenylmethyl)-1H-1,4-benzodiazepin-2-one (Example C-F)	C-G	595.1
8C-372	3-(N'-(4,4,4-Trifluorobutyryl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-ethylbutyl)-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-ethylbutyl)-1H-1,4-benzodiazepin-2-one (Example C-G)	C-G	531.2
8C-373	3-(N'-(4,4,4-Trifluorobutyryl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(cyclohexylmethyl)-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(cyclohexylmethyl)-1H-1,4-benzodiazepin-2-one (Example C-H)	C-G	543.2
8C-374	3-(N'-(4,4,4-Trifluorobutyryl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3-phenylpropyl)-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3-phenylpropyl)-1H-1,4-benzodiazepin-2-one (Example C-J)	C-G	565.1

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-375	3-(N'-(4,4,4-Trifluorobutyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-biphenylmethyl)-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-biphenylmethyl)-1H-1,4-benzodiazepin-2-one (Example C-L)	C-G	613.2
8C-376	3-(N'-(4,4,4-Trifluorobutyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3-(5-chlorobenzo[b]thienyl)methyl)-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3-(5-chlorobenzo[b]thienyl)methyl)-1H-1,4-benzodiazepin-2-one (Example C-O)	C-G	627.1
8C-377	3-(N'-(4,4,4-Trifluorobutyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-1H-1,4-benzodiazepin-2-one (Example C-P)	C-G	545.2
8C-378	3-(N'-(4,4,4-Trifluorobutyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(5-benzofurazanylmethyl)-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(5-benzofurazanylmethyl)-1H-1,4-benzodiazepin-2-one (Example C-Q)	C-G	579.1

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-379	3-(N'-(4,4,4-Trifluorobutyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3-phenoxypropyl)-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(3-phenoxypropyl)-1H-1,4-benzodiazepin-2-one (Example C-R)	C-G	581.1
8C-380	3-(N'-(4,4,4-Trifluorobutyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(6-(2-trifluoromethylquinolinyl)methyl)-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(6-(2-trifluoromethylquinolinyl)methyl)-1H-1,4-benzodiazepin-2-one (Example C-S)	C-G	656.1
8C-381	3-(N'-(4,4,4-Trifluorobutyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(cyclopropylmethyl)-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(cyclopropylmethyl)-1H-1,4-benzodiazepin-2-one (Example 8-L)	C-G	501.1
8C-382	3-(N'-(4,4,4-Trifluorobutyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-methylbutyl)-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-methylbutyl)-1H-1,4-benzodiazepin-2-one (Example C-T)	C-G	517.2
8C-383	3-(N'-(4,4,4-Trifluorobutyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(ethyl)-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(ethyl)-1H-1,4-benzodiazepin-2-one (Example C-U)	C-G	475.1

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-384	3-(N'-(4,4,4-Trifluorobutyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(4-(3,5-dimethylisoxazolyl)methyl)-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(4-(3,5-dimethylisoxazolyl)methyl)-1H-1,4-benzodiazepin-2-one (Example C-Y)	C-G	556.1
8C-385	3-(N'-(4,4,4-Trifluorobutyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(propyl)-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(propyl)-1H-1,4-benzodiazepin-2-one (Example 8-L)	C-G	489.1
8C-386	3-(N'-(4,4,4-Trifluorobutyl)-L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-methoxyethyl)-1H-1,4-benzodiazepin-2-one	4,4,4-Trifluorobutyric acid (Fluorochem)	3-(L-alaninyl)amino-5-phenyl-2,3-dihydro-1-(2-methoxyethyl)-1H-1,4-benzodiazepin-2-one (Example C-Z)	C-G	505.1
8C-387	3-(N'-(L-(+)-Mandelyl)-L-alaninyl)amino-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	L-(+)-Mandelic acid (Sigma)	3-(L-alaninyl)amino-2,4-dioxo-1,5-bis-(2,2-dimethylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine (Example 8-L)	C-E	537.3
8C-388	(S)-3-(N'-(N-pyrrolidinylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	Pyrrolidine (Aldrich)	(S)-3-(N'-(chloroacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example C-AD)	C-F	

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-389	3-(N'-(o-Chlorophenoxyacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	o-Chlorophenoxyacetic acid (Lancaster)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	504.8
8C-390	3-(N'-(2-Thiopheneacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2-Thiopheneacetic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	460.8
8C-391	3-(N'-(3-(Trifluoromethyl)phenylacetic)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-(Trifluoromethyl)phenylacetic acid (Marshallton)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	523.1
8C-392	3-(N'-(p-Tolylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	p-Tolylacetic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	468.8
8C-393	3-(N'-(3-(4-Methoxyphenyl)propionyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-(4-Methoxyphenyl)propionic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	498.8

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-394	3-(N'-(3,5-Difluorophenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	491.0
8C-395	3-(N'-(m-Tolylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	m-Tolylacetic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	468.6
8C-396	3-(N'-(3-Fluorophenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-Fluorophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	472.8
8C-397	3-(N'-(3-Bromophenylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-Bromophenylacetic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	535.0
8C-398	3-(N'-(4-Chlorophenoxyacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	4-Chlorophenoxyacetic acid (Grand Island Biological Company)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	505.0
8C-399	3-(N'-(2-Naphthylacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	2-Naphthylacetic acid (Aldrich)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	505.0

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-400	3-(N'-(3-Methylphenoxyacetyl)-L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one	3-Methylphenoxyacetic acid (Lancaster)	3-(L-alaninyl)amino-2,3-dihydro-1-methyl-5-phenyl-1H-1,4-benzodiazepin-2-one (Example 8-B)	C-A	489.0

GENERAL PROCEDURE C-J

A vial was charged with a CHCl_3 solution of Starting material 1 (71 μmol), a DMF solution of HOBt monohydrate (71 μmol), a CHCl_3 solution of diisopropylcarbodiimide (71 μmol), and a CHCl_3 solution of starting material 2 (60 μmol). The vial was capped and the solution allowed to stand at room temperature for two days. The reaction mixture was loaded onto a cation exchange column, washed with MeOH and eluted with 2 N NH_3/MeOH . The eluents were concentrated and dried to give the desired product as determined by MS (IS) and HPLC.

GENERAL PROCEDURE C-K

To a 4 mL vial was added 870 μL of 0.05 mM stock solution of starting material 1 in DMF/chloroform, 1000 μL of a 0.05 mM stock solution of starting material 2 in chloroform, 1000 μL of a 0.05 mM stock solution of 1-(3-dimethylaminopropyl)-3-ethyl carbodiimide in chloroform and 100 μL of a 0.48 mM stock solution of HOBt in DMF. After standing undisturbed for 48 h, the reaction mixture was concentrated and the residue redissolved in 2 mL of a 10% methanol/methylene chloride solution. This solution was then filtered through a pre-washed (methanol) 500 mg SCX column using an additional 8 mL of the same solvent. The filtrate was concentrated under a stream of nitrogen to approximately 1/3 its original volume and then passed over a plug (200 mg) of AG 1-8x anion exchange resin (BioRad; Hercules, California; Columns were pre-washed with 1N NaOH, water and methanol) using an additional 6 mL of 10% methanol/methylene chloride solution. The resulting filtrate was concentrated under vacuum and the crude products were submitted for testing without further purification. Product structure and purity were confirmed by HPLC and IEX MS.

Example C-AE

Synthesis of

3-[(L-Alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one

Step A: **Synthesis of 3-Amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one**

The title compound was synthesized as described in *Synth. Commun.*, 26(4), 721-727 (1996).

Step B: **Synthesis of 3-[(N-tert-Butoxycarbonyl-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one**

A solution of L-Boc-alanine (1.74 g, 9.20 mmol), HOBt monohydrate (1.24 g, 9.20 mmol), diisopropylethylamine (1.6 mL, 9.20 mmol) and CH₂Cl₂ (30 mL) was purged with nitrogen and cooled in an ice bath. To the cold solution was added 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.76 g, 9.20 mmol) followed by a solution of 3-amino-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (2.45 g, 9.20 mmol) dissolved in CH₂Cl₂ (15 mL). The cold bath was removed and the solution stirred overnight at room temperature. The reaction mixture was extracted with H₂O, 0.1 N aq. citric acid, 5% aq. NaHCO₃, and brine. The remaining CH₂Cl₂ solution was dried (MgSO₄) and concentrated to a tan foam. The title compound was crystallized from CH₂Cl₂/EtOAc to give 3.47 g (86% yield) of white crystals, mp. 228-229°C.

Anal. Calcd for C₂₃H₂₇N₅O₄: C, 63.14; H, 6.22; N, 16.01. Found: C, 63.25; H, 6.15; N, 15.95. MS (FD⁺) 437 m/z.

Step C: **Synthesis of 3-[(L-Alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one**

A solution of 3-[(N-tert-butoxycarbonyl-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (3.42 g, 7.82 mmol) in CH₂Cl₂ (90 mL) was cooled in an ice bath and treated with TFA (13.2 mL, 172 mmol). The cold bath was removed and the solution stirred at room temperature for four hours. The reaction mixture was washed with 1 M aq. K₂CO₃ and the aqueous back-extracted with CH₂Cl₂. The combined extracts were washed with H₂O, dried (MgSO₄) and concentrated to obtain 1.75 g (66% yield) of the title compound as an off-white foam. MS (IS⁺) 338 (m/e).

¹HNMR (CDCl₃): δ = 8.76-8.86 (1H, m), 8.63 (1H, m), 8.17 (1H, m), 7.82 (2H, m), 7.60 (1H, m), 7.41 (3H, m), 5.60 (1H, m), 3.63 (1H, m), 3.49 (3H, s), 1.66 (2H, broad), 1.45 (3H, m).

5

Example C-AF

Synthesis of

3-[(L-Alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethylaminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one

10

Step A: Synthesis of 3-Amino-2,3-dihydro-1-(2-N,N-diethylaminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one

The title compound was synthesized as described in *Synth. Commun.*, 26(4), 721-727 (1996).

15

Step B: Synthesis of 3-[(N-tert-Butoxycarbonyl-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethylaminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one

20

A solution of L-Boc-alanine (1.80 g, 9.50 mmol), HOBT monohydrate (1.28 g, 9.50 mmol), diisopropylethylamine (1.65 mL, 9.50 mmol) and CH₂Cl₂ (40 mL) was purged with nitrogen and cooled in an ice bath. To the cold solution was added 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.82 g, 9.50 mmol) followed by a solution of 3-amino-2,3-dihydro-1-(2-N,N-diethylaminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (3.34 g, 9.50 mmol) dissolved in CH₂Cl₂ (25 mL). The cold bath was removed and the solution stirred overnight at room temperature. The reaction mixture was extracted with H₂O, 5% aq. NaHCO₃, and brine. The remaining CH₂Cl₂ solution was dried (MgSO₄) and concentrated to a tan foam. The title compound was isolated via column chromatography (2% MeOH/CH₂Cl₂ to 10% MeOH/CH₂Cl₂) to give 3.53 g (71% yield) of yellow foam.

25

30

MS (FD⁺) 522 (m/z).

¹HNMR (CDCl₃): δ = 8.62 (1H, d), 8.11 (1H, m), 7.80 (2H, m), 7.59 (2H, m), 7.32-7.45 (2H, m), 5.54 (1H, m), 5.02-5.18 (1H, m), 4.38 (1H, m),

4.20 (1H, m), 3.83 (1H, m), 2.62 (2H, t), 2.44 (4H, m), 1.40-1.56 (12H, m), 0.88 (6H, m).

5 Step C: **Synthesis of 3-[(L-Alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethylaminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one**

The title compound was synthesized using the procedure described in Example C-AE, Step C. A solution of 3-[(N-tert-butoxycarbonyl-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethylaminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (3.52 g, 6.73 mmol) was treated with TFA (11.4 mL, 148 mmol) to give 2.61 g (92% yield) the title compound as a light yellow foam.

MS (IS⁺) 423 (m/e).

¹HNMR (CDCl₃): δ = 8.78-8.93 (1H, m), 8.62 (1H, d), 8.11 (1H, m), 7.80 (2H, m), 7.58 (2H, m), 7.39 (2H, m), 5.58 (1H, m), 4.22 (1H, m), 3.88 (1H, m), 3.61 (1H, m), 2.67 (2H, t), 2.49 (4H, m), 1.73 (2H, broad), 1.42 (3H, m), 0.91 (6H, m).

Example C-AG

15 **Synthesis of 3-[(L-Alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one**

20 Step A: **Synthesis of 3-Amino-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one**

The title compound was synthesized as described in *Synth. Commun.*, 26(4), 721-727 (1996).

25 Step B: **Synthesis of 3-[(N-tert-Butoxycarbonyl-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one**

30 A solution of L-Boc-alanine (1.57 g, 8.33 mmol), HOBt monohydrate (1.13 g, 8.33 mmol), diisopropylethylamine (1.45 mL, 8.33 mmol) and CH₂Cl₂ (40 mL) was purged with nitrogen and cooled in an ice bath. To the cold solution was added 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.60 g, 8.33 mmol) followed by a solution of 3-amino-2,3-

dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (2.92 g, 8.33 mmol) dissolved in CH_2Cl_2 (25 mL). The cold bath was removed and the solution stirred overnight at room temperature. The reaction mixture was extracted with H_2O , 0.1 N aq. citric acid, 5% aq. NaHCO_3 , and brine.

5 The remaining CH_2Cl_2 solution was dried (MgSO_4) and concentrated to a yellow foam. The title compound was isolated via column chromatography (20% EtOAc/hexanes to 60% EtOAc/hexanes) to give 4.19 g (96% yield) of light yellow foam.

MS (FD^+) 521 (m/z).

10 $^1\text{HNMR}$ (CDCl_3): δ = 8.65 (1H, t), 8.17 (1H, t), 7.90 (1H, t), 7.71-7.85 (1H, m), 7.54 (1H, m), 7.44 (1H, t), 7.37 (1H, d), 7.24-7.32 (1H, m), 7.14 (1H, m), 5.67 (1H, dd), 5.18 (1H, broad), 4.93-5.07 (1H, m), 4.50-4.64 (1H, m), 4.38 (1H, broad), 1.42-1.51 (12H, m), 1.26 (9H, d).

15 Step C: **Synthesis of 3-[(L-Alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one**

The title compound was synthesized using the procedure described in Example C-AE, Step C. A solution of 3-[(N-tert-butoxycarbonyl-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (4.18 g, 8.01 mmol) was treated with TFA (13.6 mL, 176 mmol) to give 3.14 g (93% yield) the title compound as an off-white foam.

MS (IS^+) 422 (m/e).

25 $^1\text{HNMR}$ (CDCl_3) δ 8.85-8.99 (1H, m), 8.68 (1H, d), 8.20 (1H, t), 7.87 (1H, t), 7.58 (1H, t), 7.42 (2H, m), 7.30 (1H, t), 7.17 (1H, d), 5.72 (1H, m), 5.08 (1H, d), 4.60 (1H, d), 3.66 (1H, m), 1.47 (3H, m), 1.28 (9H, m).

Example C-AH

30 **Synthesis of 3-[(L-Alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-thiazyl)-1H-1,4-benzodiazepin-2-one**

Step A: **Synthesis of 3-Amino-2,3-dihydro-1-methyl-5-(2-thiazyl)-1H-1,4-benzodiazepin-2-one**

The title compound was synthesized in a manner similar to the procedure described in *Synth. Commun.*, 26(4), 721-727 (1996), starting with 2-(2-aminobenzoyl)thiazole (prepared as described in *Tetrahedron*, 51(3), 773-786, (1995)).

5 MS (IS⁺) 273 (m/e).

¹HNMR (CDCl₃): δ = 7.83-7.94 (2H, m), 7.61 (1H, t), 7.50 (1H, d), 7.34 (2H, m), 4.60 (1H, s), 3.46 (3H, s), 1.97 (2H, broad).

10 Step B: **Synthesis of 3-[(N-tert-Butoxycarbonyl-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-thiazyl)-1H-1,4-benzodiazepin-2-one**

A solution of L-Boc-alanine (1.85 g, 9.77 mmol), HOBt monohydrate (1.32 g, 9.77 mmol), diisopropylethylamine (1.70 mL, 9.77 mmol) and CH₂Cl₂ (30 mL) was purged with nitrogen and cooled in an ice bath. To the cold solution was added 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.87 g, 9.77 mmol) followed by a solution of 3-amino-2,3-dihydro-1-methyl-5-(2-thiazyl)-1H-1,4-benzodiazepin-2-one (2.66 g, 9.77 mmol) dissolved in CH₂Cl₂ (20 mL). The cold bath was removed and the solution stirred overnight at room temperature. The reaction mixture was extracted with H₂O, 0.1 N aq. citric acid, 5% aq. NaHCO₃, and brine. The remaining CH₂Cl₂ solution was dried (MgSO₄) and concentrated to a light yellow foam. The title compound was crystallized from EtOAc/hexane to give 3.22 g (74% yield) of white crystals, mp. 196-197°C. Anal. Calcd for C₂₁H₂₅N₅O₄S: C, 56.87; H, 5.68; N, 15.79. Found: C, 56.74; H, 5.75; N, 15.55.

25 MS (IS⁺) 444 m/e.

Step C: **Synthesis of 3-[(L-Alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-thiazyl)-1H-1,4-benzodiazepin-2-one**

30 The title compound was synthesized using the procedure described in Example C-AE, Step C.

Example C-AI

Synthesis of

3-[(L-Alaninyl)amino]-2,3-dihydro-1-methyl-5-(thiophen-2-yl)-1H-1,4-benzodiazepin-2-one

5 Step A: Synthesis of 3-Amino-2,3-dihydro-1-methyl-5-(2-thiophen-2-yl)-1H-1,4-benzodiazepin-2-one

The title compound was synthesized in a manner similar to the procedure described in *Synth. Commun.*, **26**(4), 721-727 (1996), starting with 2-(2-aminobenzoyl)thiophene (prepared as described in *Collect. Czech. Chem. Commun.*, **34**(2), 468-478, (1969)).

MS (IS⁺) 272 (m/e).

¹HNMR (CDCl₃): δ = 7.68 (1H, d), 7.60 (1H, t), 7.48 (1H, m), 7.35 (2H, d), 7.28 (1H, m), 7.15 (1H, d), 7.05 (1H, d), 4.50 (1H, broad), 3.45 (3H, s), 2.26 (2H, broad).

Step B: **Synthesis of 3-[(N-tert-Butoxycarbonyl-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-thiophenyl)-1H-1,4-benzodiazepin-2-one**

20 The title compound was synthesized in a manner similar to the procedure described in Example C-AH, Step B.

MS (IS⁺) 443 (m/e).

¹HNMR (CDCl₃): δ = 7.69 (1H, d), 7.61 (2H, m), 7.48 (1H, d), 7.27-7.42 (2H, m), 7.18 (1H, m), 7.05 (1H, m), 5.51 (1H, d), 5.13 (1H, broad), 4.36 (1H, broad), 3.44 (3H, s), 1.38-1.57 (12H, m).

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Step C: **Synthesis of 3-[(L-Alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-thiophenyl)-1H-1,4-benzodiazepin-2-one**

The title compound was synthesized in a manner similar to the procedure described in Example C-AE, Step C.

30 MS (IS⁺) 343 (m/e).

¹HNMR (CDCl₃): δ = 8.55 (1H, d), 7.68 (1H, d), 7.59 (1H, m), 7.48 (1H, d), 7.36 (1H, d), 7.31 (1H, d), 7.16 (1H, m), 7.04 (1H, t), 5.54 (1H, d), 3.58 (1H, m), 3.45 (3H, s), 1.41 (3H, d).

Using the procedures indicated, the compounds shown in Table C-2 were prepared.

Table C-2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-401	3-[(N'-(4-methoxyphenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-Methoxyphenylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	485.5
8C-402	3-[(N'-(2-thiopheneacetyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	2-Thiopheneacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	461.5
8C-403	3-[(N'-(3,5-difluorophenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	491.5
8C-404	3-[(N'-(3-bromophenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	3-Bromophenylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	534.4
8C-405	3-[(N'-(phenylmercaptoacetyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	Phenylmercaptoacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	487.6

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-406	3-[(N'-(4-ethoxyphenylacetyl))-L-alaninyl]amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-Ethoxyphenylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	499.6
8C-407	3-[(N'-(4-(trifluoromethyl)phenylacetyl))-L-alaninyl]amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-(trifluoromethyl)phenylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	523.5
8C-408	3-[(N'-(3,5-bis(trifluoromethyl)phenylacetyl))-L-alaninyl]amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	3,5-bis(trifluoromethyl)phenylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	591.5
8C-409	3-[(N'-(methylthioacetyl))-L-alaninyl]amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	(methylthio)acetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	425.5
8C-410	3-[(N'-(cyclohexylacetyl))-L-alaninyl]amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	cyclohexylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	461.6

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-411	3-[(N'-(pentafluorophenoxyacetyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	pentafluorophenoxyacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	561.5
8C-412	3-[(N'-(benzo[b]thiophene-3-acetyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	benzo [b] thiophene-3-acetic acid (Lancaster)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	511.6
8C-413	3-[(N'-(2,4,6-trimethylphenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	2,4,6-trimethylphenylacetic acid (Lancaster)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	497.6
8C-414	3-[(N'-(4-biphenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-biphenylacetic acid (Lancaster)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	531.6
8C-415	3-[(N'-(3,4-difluorophenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	3,4-difluorophenylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	491.5

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-416	3-[(N'-(4-(2-thienyl)butyryl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-(2-thienyl)butyric acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	489.6
8C-417	3-[(N'-(5-methylhexanoyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	5-methylhexanoic acid (P&B)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	449.5
8C-418	3-[(N'-(3-methoxycarbonylpropionyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	mono-methyl succinate (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	451.5
8C-419	3-[(N'-(methanesulfonylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	methanesulfonylacetic acid (Lancaster)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	457.5
8C-420	3-[(N'-(4-toluenesulfonylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-toluenesulfonylacetic acid (Lancaster)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	533.6

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-421	3-[(N'-(2,6-difluoromandelyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	2,6-difluoromandelic acid (Fluorochem)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	507.5
8C-422	3-[(N'-(4-fluoromandelyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-fluoromandelic acid (Lancaster)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	489.5
8C-423	3-[(N'-(2,5-difluoromandelyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	2,5-difluoromandelic acid (Fluorochem)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	507.5
8C-424	3-[(N'-(2,4,6-trifluorophenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	2,4,6-trifluorophenylacetic acid (Fluorochem)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	509.5
8C-425	3-[(N'-(4-fluoro-2-(trifluoromethyl)phenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-fluoro-2-(trifluoromethyl)phenylacetic acid (Fluorochem)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	541.5

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-426	3-[(N'-(4,4,4-trifluorobutyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4,4,4-trifluorobutyric acid (Fluorochem)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	461.4
8C-427	3-[(N'-(4-isopropylphenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-isopropylphenylacetic acid (Lancaster)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	497.6
8C-428	3-[(N'-(beta-phenyllactyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	beta-phenyllactic acid (Sigma)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	485.5
8C-429	3-[(N'-(mandelyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	mandelic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	471.5
8C-430	3-[(N'-(4-chloromandelyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	p-chloromandelic acid (Acros)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	506.0
8C-431	3-[(N'-(isovaleryl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	isovaleric acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	421.5

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-432	3-[(N'-(2,3,5-trifluorophenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	2,3,5-trifluorophenylacetic acid (Fluorochem)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	509.5
8C-433	3-[(N'-(3-methylthiopropionyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	3-methylthiopropionic acid (Lancaster)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	439.5
8C-434	3-[(N'-(L-alpha-hydroxyisocaproyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	L-alpha-hydroxyisocaproic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	451.5
8C-435	3-[(N'-(3-nitrophenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	3-nitrophenylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	500.5
8C-436	3-[(N'-(D-3-phenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	D-3-phenylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-methyl-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AE)	C-J	485.5

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-437	3-[(N'-(4-methoxyphenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-Methoxyphenylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	569.6
8C-438	3-[(N'-(2-thiopheneacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	2-Thiopheneacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	545.6
8C-439	3-[(N'-(3,5-difluorophenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	575.6
8C-440	3-[(N'-(3-bromophenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	3-Bromophenylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	618.5

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-441	3-[(N'-(phenylmercaptoacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	Phenylmercaptoacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	571.7
8C-442	3-[(N'-(4-ethoxyphenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-Ethoxyphenylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	583.7
8C-443	3-[(N'-(4-(trifluoromethyl)phenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-(trifluoromethyl)phenylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	607.6
8C-444	3-[(N'-(3,5-bis(trifluoromethyl)phenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	3,5-Bis(trifluoromethyl)phenylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	675.6

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-445	3-[(N'-(methylthio)acetyl)-L-alaninyl]amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	(methylthio)acetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	509.6
8C-446	3-[(N'-(cyclohexylacetyl)-L-alaninyl]amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	cyclohexylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	545.7
8C-447	3-[(N'-(pentafluorophenoxyacetyl)-L-alaninyl]amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	pentafluorophenoxyacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	645.6
8C-448	3-[(N'-(benzo[b]thiophene-3-acetyl)-L-alaninyl]amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	benzo [b] thiophene-3-acetic acid (Lancaster)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	595.7

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-449	3-[(N'-(2,4,6-trimethylphenylacetyl))-L-alaninyl]amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	2,4,6-trimethylphenylacetic acid (Lancaster)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	581.7
8C-450	3-[(N'-(4-biphenylacetyl))-L-alaninyl]amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-biphenylacetic acid (Lancaster)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	615.7
8C-451	3-[(N'-(3,4-difluorophenylacetyl))-L-alaninyl]amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	3,4-difluorophenylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	575.6
8C-452	3-[(N'-(4-(2-thienyl)butyl))-L-alaninyl]amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-(2-thienyl)butyric acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	573.7

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-453	3-[(N'-(5-methylhexanoyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	5-methylhexanoic acid (P&B)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	533.7
8C-454	3-[(N'-(3-methoxycarbonylpropionyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	mono-methyl succinate (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	C-J	535.6
8C-455	3-[(N'-(methanesulfonylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	methanesulfonylacetic acid (Lancaster)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	541.6
8C-456	3-[(N'-(4-toluenesulfonylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-toluenesulfonylacetic acid (Lancaster)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	617.7

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-457	3-[(N'-(2,6-difluoromandelyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	2,6-difluoromandelic acid (Fluorochem)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	591.6
8C-458	3-[(N'-(4-fluoromandelyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-fluoromandelic acid (Lancaster)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	573.6
8C-459	3-[(N'-(2,5-difluoromandelyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	2,5-difluoromandelic acid (Fluorochem)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	591.6
8C-460	3-[(N'-(2,4,6-trifluorophenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	2,4,6-trifluorophenylacetic acid (Fluorochem)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	593.6

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-461	3-[(N'-(4-fluoro-2-(trifluoromethyl)phenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-fluoro-2-(trifluoromethyl)phenylacetic acid (Fluorochem)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	625.6
8C-462	3-[(N'-(4,4,4-trifluorobutyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4,4,4-trifluorobutyric acid (Fluorochem)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	545.5
8C-463	3-[(N'-(4-isopropylphenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-isopropylphenylacetic acid (Lancaster)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	581.7
8C-464	3-[(N'-(beta-phenyllactyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	beta-phenyllactic acid (Sigma)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	569.6

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-465	3-[(N'-(mandelyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	mandelic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	555.6
8C-466	3-[(N'-(4-chloromandelyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	p-chloromandelic acid (Acros)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	590.1
8C-467	3-[(N'-(isovaleryl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	isovaleric acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	505.6
8C-468	3-[(N'-(2,3,5-trifluorophenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	2,3,5-trifluorophenylacetic acid (Fluorochem)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	593.6

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-469	3-[(N'-(3-methylthiopropionyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	3-methylthiopropionic acid (Lancaster)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	523.6
8C-470	3-[(N'-(L-alpha-hydroxyisocaproyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	L-alpha-hydroxyisocaproic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	535.6
8C-471	3-[(N'-(3-nitrophenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	3-nitrophenylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	584.6
8C-472	3-[(N'-(D-3-phenyllactyl)-L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	D-3-phenyllactic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(3,3-dimethyl-2-oxobutyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AG)	C-J	569.6

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-473	3-[(N'-(4-methoxyphenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-Methoxyphenylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	570.7
8C-474	3-[(N'-(2-thiopheneacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	2-Thiopheneacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	546.7
8C-475	3-[(N'-(N"-acetyl-N"-phenylglycyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	N-acetyl-N-phenylglycine (Kodak)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	597.7
8C-476	3-[(N'-(3,5-difluorophenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	3,5-Difluorophenylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	576.6

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-477	3-[(N'-(3-bromophenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	3-Bromophenylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	619.6
8C-478	3-[(N'-(phenylmercaptoacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	Phenylmercaptoacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	572.7
8C-479	3-[(N'-(4-ethoxyphenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-Ethoxyphenylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	584.7
8C-480	3-[(N'-(4-(trifluoromethyl)phenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-(trifluoromethyl)phenylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	608.7

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-481	3-[(N'-(3,5-bis(trifluoromethyl)phenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	3,5-Bis(trifluoromethyl)phenylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	676.7
8C-482	3-[(N'-(methylthioacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	(methylthio)acetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	510.6
8C-483	3-[(N'-(cyclohexylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	cyclohexylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	546.7
8C-484	3-[(N'-(pentafluorophenoxyacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	pentafluorophenoxyacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	646.6

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-485	3-[(N'-(benzo[b]thiophene-3-acetyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	benzo [b] thiophene-3-acetic acid (Lancaster)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	596.7
8C-486	3-[(N'-(benzoylformyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	benzoylformic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	554.6
8C-487	3-[(N'-(2,4,6-trimethylphenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	2,4,6-trimethylphenylacetic acid (Lancaster)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	582.7
8C-488	3-[(N'-(4-biphenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-biphenylacetic acid (Lancaster)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	616.8

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-489	3-[(N'-(3,4-difluorophenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	3,4-difluorophenylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	576.6
8C-490	3-[(N'-(4-(2-thienyl)butyryl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-(2-thienyl)butyric acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	574.7
8C-491	3-[(N'-(5-methylhexanoyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	5-methylhexanoic acid (P&B)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	534.7
8C-492	3-[(N'-(3-methoxycarbonylpropionyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	mono-methyl succinate (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	536.6

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-493	3-[(N'-(methanesulfonylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	methanesulfonylacetic acid (Lancaster)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	542.6
8C-494	3-[(N'-(4-toluenesulfonylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-toluenesulfonylacetic acid (Lancaster)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	618.7
8C-495	3-[(N'-(2,6-difluoromandelyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	2,6-difluoromandelic acid (Fluorochem)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	592.6
8C-496	3-[(N'-(4-fluoromandelyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-fluoromandelic acid (Lancaster)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	574.6

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-497	3-[(N'-(2,5-difluoromandelyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	2,5-difluoromandelic acid (Fluorochem)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	592.6
8C-498	3-[(N'-(4-(hydroxymethyl)phenoxyacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-(hydroxymethyl)phenoxyacetic acid (Sigma)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	586.7
8C-499	3-[(N'-(2,4,6-trifluorophenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	2,4,6-trifluorophenylacetic acid (Fluorochem)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	594.6
8C-500	3-[(N'-(4-fluoro-2-(trifluoromethyl)phenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-fluoro-2-(trifluoromethyl)phenylacetic acid (Fluorochem)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	626.6

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-501	3-[(N'-(4,4,4-trifluorobutyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4,4,4-trifluorobutyric acid (Fluorochem)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	546.6
8C-502	3-[(N'-(4-isopropylphenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	4-isopropylphenylacetic acid (Lancaster)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	582.7
8C-503	3-[(N'-(beta-phenyllactyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	beta-phenyllactic acid (Sigma)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	570.7
8C-504	3-[(N'-(mandelyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	mandelic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)- 5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	556.7

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-505	3-[(N'-(4-chloromandelyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	p-chloromandelic acid (Acros)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	591.1
8C-506	3-[(N'-(isovaleryl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	isovaleric acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	506.6
8C-507	3-[(N'-(2,3,5-trifluorophenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	2,3,5-trifluorophenylacetic acid (Fluorochem)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	594.6
8C-508	3-[(N'-(3-methylthiopropionyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	3-methylthiopropionic acid (Lancaster)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	524.7

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-509	3-[(N'-(L-alpha-hydroxyisocaproyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	L-alpha-hydroxyisocaproic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	536.7
8C-510	3-[(N'-(3-nitrophenylacetyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	3-nitrophenylacetic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	585.7
8C-511	3-[(N'-(D-3-phenyllactyl)-L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one	D-3-phenyllactic acid (Aldrich)	3-[(L-alaninyl)amino]-2,3-dihydro-1-(2-N,N-diethyl aminoethyl)-5-(2-pyridyl)-1H-1,4-benzodiazepin-2-one (Example C-AF)	C-J	570.7

GENERAL PROCEDURE C-L

The following amino acids were employed in this procedure: L-alanine (Aldrich), L-valine (Aldrich), L-norvaline (Aldrich), L-methionine (Aldrich), L-phenylalanine (Aldrich), L-(+)- α -phenylglycine (Aldrich), L- α -(2-thienyl)glycine (Sigma), L- α -(3-thienyl)glycine (Sigma), L-cyclohexylglycine hydrochloride (Senn Chemical AG), *O*-*tert*-butyl-L-serine (Sigma), *O*-*tert*-butyl-L-threonine (Bachem) and *O*-*tert*-butyl-L-tyrosine (Bachem).

The amino acid (60 μ moles), 305 mg (150 μ moles) of N,O-bis(trimethylsilyl)acetamide and 1.5 mL of DMF were introduced into separate fritted screw capped vials. The mixtures were heated mildly and upon cooling 132 mg (15 μ moles) of p-nitrophenylcarbonate Wang resin (actual load of 1.14 mmole/g) (Novabiochem) was added to the individual vials. In addition, 73 mg (60 μ moles) of dimethylaminopyridine was introduced into vials containing L-cyclohexylglycine hydrochloride. The vials were shaken at room temperature for 48 hours. Each reaction mixture was filtered through the internal frit and the resulting resin was washed with (9 x 1.0 mL) of DMF, (9 x 1.0 mL) of methanol and (6 x 1.0 mL) of diethyl ether. Each reaction vial containing the resin bound amino acid was then dried in a vacuum oven at 30°C.

GENERAL PROCEDURE C-M

Into each fritted screw capped vial containing a resin bound amino acid (from General Procedure C-L) was introduced 81 mg (60 μ moles) of 1-hydroxybenzotriazole hydrate (HOBt H_2O), 115 mg (60 μ moles) of 1-(3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride (EDC HCl), and 2 mL of THF. A 3-amino-2,4-dioxo-1,5-bis-(alkyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepin (30 μ moles) selected from 3-amino-2,4-dioxo-1,5-bis(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepin (Example 8S, Step C), 3-amino-2,4-dioxo-1,5-bis(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepin (Example 8-R, Step C) and 3-amino-2,4-dioxo-1,5-bis(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepin (Example 8-U, Step C) was added to

the vials. Each vial was then capped and shaken at room temperature for 4 days. Each reaction mixture was filtered through the internal frit and the resulting resin was washed with (3 x 2.0 mL) of DMF, (3 x 2.0 mL) of a 10 % solution of acetic acid in methanol, (3 x 2.0 mL) of a 10 % solution of acetic acid in THF, and (3 x 2.0 mL) of a 10 % solution of acetic acid in dichloromethane.

GENERAL PROCEDURE C-N

Each resin from General Procedure C-M was suspended in 2.0 mL of trifluoroacetic acid for 30 minutes. Each reaction was filtered through the internal frit into a 10 mL vial and the resin was washed with (3 x 1.0 mL) of methanol. The filtrate was concentrated under a flow of nitrogen at 30°C. The concentrated residue was dissolved in 1.5 mL of methanol and partitioned into 3 portions. Each portion was subjected to affinity chromatography on a pretreated SCX column (pretreatment consisted of flushing with 2 mL of a 10 % solution of acetic acid in methanol followed by 2 mL of methanol). Once loaded, all columns were flushed with 5 mL of methanol, discarding each wash. Each compound was liberated from the column with 5 mL of a 1 N solution of ammonia in a 1/1 solution of methanol and chloroform. Each solution was transferred to a tarred vial followed by concentration under a stream of nitrogen, followed by final concentration under vacuum.

GENERAL PROCEDURE C-O

To each vial containing a specific amino acid benzodiazepine (from General Procedure C-N) was added 1 mL of a 0.4 M solution of 1-(3-dimethylaminopropyl)-3-ethyl-carbodiimide (EDC) and 0.9 equivalents of a carboxylic acid selected from 3,5-difluorophenylacetic acid, cyclopentylacetic acid and 4,4,4-trifluorophenylacetic acid. The vials were capped and shaken for 4 days. Each reaction was then concentrated under a continuous flow of nitrogen. The residue was subjected to affinity chromatography on a pretreated SCX column (pretreatment consisted of flushing with 2 mL of a 10 % solution

of acetic acid in methanol followed by 2 mL of methanol). Once loaded, all columns were eluted with 5 mL of methanol. Each solution was transferred to a tarred vial followed by concentration under a stream of nitrogen with final concentration under vacuum:

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Using the procedures indicated, the compounds shown in Table C-3 were prepared. In this table, Starting Material 1 was prepared using General Procedures C-L, C-M and C-N. 3,5-Difluorophenylacetic acid and cyclopentylacetic acid are available from Aldrich, and 4,4,4-trifluorobutyric acid is available from Fluorochem.

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Table C-3

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-512	3-[N-(3,5-Difluorophenylacetyl)-L-alaninyl]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Alaninyl)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	529.2
8C-513	3-[N-(3,5-Difluorophenylacetyl)-L-alaninyl]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Alaninyl)-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	445.1
8C-514	3-[N-(3,5-Difluorophenylacetyl)-L-alaninyl]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Alaninyl)-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	525.2
8C-515	3-[N-(3,5-Difluorophenylacetyl)-L-valinyl]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Valinyl)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	557.3
8C-516	3-[N-(3,5-Difluorophenylacetyl)-L-valinyl]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Valinyl)-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	473.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-517	3-[N-(3,5-Difluorophenylacetyl)-L-valinyl]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Valinyl)-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	553.2
8C-518	3-[N-(3,5-Difluorophenylacetyl)-L-norvalinyl]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Norvalinyl)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	557.3
8C-519	3-[N-(3,5-Difluorophenylacetyl)-L-norvalinyl]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Norvalinyl)-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	473.2
8C-520	3-[N-(3,5-Difluorophenylacetyl)-L-norvalinyl]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Norvalinyl)-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	553.2
8C-521	3-[N-(3,5-Difluorophenylacetyl)-L-methioninyl]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Methioninyl)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	587.3
8C-522	3-[N-(3,5-Difluorophenylacetyl)-L-methioninyl]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Methioninyl)-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	503.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-523	3-[N-(3,5-Difluorophenylacetyl)-L-methioninyl]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Methioninyl)-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	583.2
8C-524	3-[N-(3,5-Difluorophenylacetyl)-L-phenylalaninyl]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Phenylalaninyl)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	603.3
8C-525	3-[N-(3,5-Difluorophenylacetyl)-L-phenylalaninyl]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Phenylalaninyl)-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	519.2
8C-526	3-[N-(3,5-Difluorophenylacetyl)-L-phenylalaninyl]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Phenylalaninyl)-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	601.2
8C-527	3-[N-(3,5-Difluorophenylacetyl)-L-phenylglycinyl]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Phenylglycinyl)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	591.3
8C-528	3-[N-(3,5-Difluorophenylacetyl)-L-phenylglycinyl]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Phenylglycinyl)-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	507.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-529	3-[N-(3,5-Difluorophenylacetyl)-L-phenylglycine]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Phenylglycine)-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	587.2
8C-530	3-[N-(3,5-Difluorophenylacetyl)-(2-thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-[(2-Thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	597.2
8C-531	3-[N-(3,5-Difluorophenylacetyl)-(2-thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-[(2-Thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	513.1
8C-532	3-[N-(3,5-Difluorophenylacetyl)-(2-thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-[(2-Thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	593.2
8C-533	3-[N-(3,5-Difluorophenylacetyl)-(3-thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-[(3-Thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	597.2
8C-534	3-[N-(3,5-Difluorophenylacetyl)-(3-thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-[(3-Thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	513.1

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-535	3-[N-(3,5-Difluorophenylacetyl)-(3-thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-[(3-Thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	593.2
8C-536	3-[N-(3,5-Difluorophenylacetyl)-L-threoninyl]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Threoninyl)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	559.3
8C-537	3-[N-(3,5-Difluorophenylacetyl)-L-threoninyl]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Threoninyl)-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	475.2
8C-538	3-[N-(3,5-Difluorophenylacetyl)-L-threoninyl]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Threoninyl)-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	555.2
8C-539	3-[N-(3,5-Difluorophenylacetyl)-L-tyrosinyl]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Tyrosinyl)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	621.3
8C-540	3-[N-(3,5-Difluorophenylacetyl)-L-tyrosinyl]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Tyrosinyl)-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	537.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-541	3-[N-(3,5-Difluorophenylacetyl)-L-tyrosinyl]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Tyrosinyl)-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3,5-Difluorophenylacetic Acid	C-O	617.3
8C-542	3-[N-(Cyclopentylacetyl)-L-alaninyl]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Alaninyl)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	485.3
8C-543	3-[N-(Cyclopentylacetyl)-L-alaninyl]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Alaninyl)-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	401.2
8C-544	3-[N-(Cyclopentylacetyl)-L-alaninyl]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Alaninyl)-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	481.3
8C-545	3-[N-(Cyclopentylacetyl)-L-valinyl]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Valinyl)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	513.3
8C-546	3-[N-(Cyclopentylacetyl)-L-valinyl]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Valinyl)-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	429.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-547	3-[N-(Cyclopentylacetyl)-L-norvalinyl]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Valinyl)-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	509.3
8C-548	3-[N-(Cyclopentylacetyl)-L-norvalinyl]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Norvalinyl)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	513.3
8C-549	3-[N-(Cyclopentylacetyl)-L-norvalinyl]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Norvalinyl)-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	429.2
8C-550	3-[N-(Cyclopentylacetyl)-L-norvalinyl]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Norvalinyl)-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	509.3
8C-551	3-[N-(Cyclopentylacetyl)-L-methioninyl]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Methioninyl)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	545.3
8C-552	3-[N-(Cyclopentylacetyl)-L-methioninyl]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Methioninyl)-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	461.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-553	3-[N-(Cyclopentylacetyl)-L-methioninyl]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Methioninyl)-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	541.3
8C-554	3-[N-(Cyclopentylacetyl)-L-phenylalaninyl]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Phenylalaninyl)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	561.3
8C-555	3-[N-(Cyclopentylacetyl)-L-phenylalaninyl]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Phenylalaninyl)-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	477.2
8C-556	3-[N-(Cyclopentylacetyl)-L-phenylalaninyl]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Phenylalaninyl)-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	557.3
8C-557	3-[N-(Cyclopentylacetyl)-L-phenylglycinyl]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Phenylglycinyl)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	547.3
8C-558	3-[N-(Cyclopentylacetyl)-L-phenylglycinyl]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Phenylglycinyl)-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	463.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-559	3-[N-(Cyclopentylacetyl)-L-phenylglycine]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Phenylglycine)-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	543.3
8C-560	3-[N-(Cyclopentylacetyl)-(2-thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(2-methyl-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-[(2-Thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	551.3
8C-561	3-[N-(Cyclopentylacetyl)-(2-thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-[(2-Thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	469.2
8C-562	3-[N-(Cyclopentylacetyl)-(2-thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-[(2-Thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	549.2
8C-563	3-[N-(Cyclopentylacetyl)-(3-thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(2-methyl-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-[(3-Thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	553.3
8C-564	3-[N-(Cyclopentylacetyl)-(3-thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-[(3-Thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	469.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-565	3-[N-(Cyclopentylacetyl)-(3-thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-[(3-Thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	549.2
8C-566	3-[N-(Cyclopentylacetyl)-L-serinyl]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Serinyl)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	417.2
8C-567	3-[N-(Cyclopentylacetyl)-L-threoninyl]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Threoninyl)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	515.3
8C-568	3-[N-(Cyclopentylacetyl)-L-threoninyl]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Threoninyl)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	431.2
8C-569	3-[N-(Cyclopentylacetyl)-L-threoninyl]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Threoninyl)-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	511.3
8C-570	3-[N-(Cyclopentylacetyl)-L-tyrosinyl]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Tyrosinyl)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	577.3

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-571	3-[N-(Cyclopentylacetyl)-L-tyrosinyl]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Tyrosinyl)-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	493.2
8C-572	3-[N-(Cyclopentylacetyl)-L-tyrosinyl]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Tyrosinyl)-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	Cyclopentylacetic Acid	C-O	573.3
8C-573	3-[N-(4,4,4-Trifluorobutyl)-L-alaninyl]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Alaninyl)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	499.2
8C-574	3-[N-(4,4,4-Trifluorobutyl)-L-alaninyl]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Alaninyl)-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	415.1
8C-575	3-[N-(4,4,4-Trifluorobutyl)-L-alaninyl]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Alaninyl)-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	495.2
8C-576	3-[N-(4,4,4-Trifluorobutyl)-L-valinyl]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Valinyl)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	527.3

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-577	3-[N-(4,4,4-Trifluorobutyl)-L-valinyl]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Valinyl)-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	443.2
8C-578	3-[N-(4,4,4-Trifluorobutyl)-L-valinyl]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Valinyl)-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	523.2
8C-579	3-[N-(4,4,4-Trifluorobutyl)-L-norvalinyl]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Norvalinyl)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	527.3
8C-580	3-[N-(4,4,4-Trifluorobutyl)-L-norvalinyl]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Norvalinyl)-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	443.2
8C-581	3-[N-(4,4,4-Trifluorobutyl)-L-norvalinyl]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Norvalinyl)-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	523.2
8C-582	3-[N-(4,4,4-Trifluorobutyl)-L-methioninyl]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Methioninyl)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	559.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-583	3-[N-(4,4,4-Trifluorobutryl)-L-methioninyl]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Methioninyl)-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	475.1
8C-584	3-[N-(4,4,4-Trifluorobutryl)-L-methioninyl]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Methioninyl)-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	555.2
8C-585	3-[N-(4,4,4-Trifluorobutryl)-L-phenylalaninyl]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Phenylalaninyl)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	475.3
8C-586	3-[N-(4,4,4-Trifluorobutryl)-L-phenylalaninyl]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Phenylalaninyl)-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	491.2
8C-587	3-[N-(4,4,4-Trifluorobutryl)-L-phenylalaninyl]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Phenylalaninyl)-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	571.2
8C-588	3-[N-(4,4,4-Trifluorobutryl)-phenylglycinyl]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(Phenylglycinyl)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	561.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-589	3-[N-(4,4,4-Trifluorobutryl)-L-phenylglycyl]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Phenylglycyl)-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	477.1
8C-590	3-[N-(4,4,4-Trifluorobutryl)-L-(2-thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-[L-(2-Thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	567.2
8C-591	3-[N-(4,4,4-Trifluorobutryl)-L-(2-thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-[L-(2-Thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	483.1
8C-592	3-[N-(4,4,4-Trifluorobutryl)-L-(2-thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-[L-(2-Thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	563.2
8C-593	3-[N-(4,4,4-Trifluorobutryl)-L-(3-thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-[L-(3-Thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	567.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-594	3-[N-(4,4,4-Trifluorobutyl)-L-(3-thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-[L-(3-Thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	483.1
8C-595	3-[N-(4,4,4-Trifluorobutyl)-L-(3-thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-[L-(3-Thienyl)glycine]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	563.2
8C-596	3-[N-(4,4,4-Trifluorobutyl)-L-cyclohexylglycine]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Cyclohexylglycine)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	567.3
8C-597	3-[N-(4,4,4-Trifluorobutyl)-L-cyclohexylglycine]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Cyclohexylglycine)-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	483.2
8C-598	3-[N-(4,4,4-Trifluorobutyl)-L-cyclohexylglycine]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Cyclohexylglycine)-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	563.3

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
8C-599	3-[N-(4,4,4-Trifluorobutyl)-L-threoninyl]-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Cyclohexylglycyl)-amino-2,4-dioxo-1,5-bis-(2-methylpropyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	527.3
8C-600	3-[N-(4,4,4-Trifluorobutyl)-L-threoninyl]-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Cyclohexylglycyl)-amino-2,4-dioxo-1,5-bis-(methyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	445.2
8C-601	3-[N-(4,4,4-Trifluorobutyl)-L-threoninyl]-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	3-(L-Cyclohexylglycyl)-amino-2,4-dioxo-1,5-bis-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine	4,4,4-Trifluorobutyric Acid	C-O	525.2

GENERAL PROCEDURE C-P

A solution of the carboxylic acid (0.75 mL, 0.05 M in DCM) was reacted with L-alaninyl-5-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one (0.75 mL, 0.06 M in DCM) (from Example 7-I), PP-HOBT (0.3 mL, 0.15 M in DMF, this reagent was used only with alpha substituted carboxylic acids), and EDC (0.3 mL, 0.15 M). The reaction was mixed for 18 hours, then purified on a Varian SCX column (500 mg column prewashed with MeOH (3 x 2.5 mL) and 20% MeOH:DCM (3 x 2.5 mL)) eluting with 2.5 mL of 20% MeOH:DCM.

GENERAL PROCEDURE C-Q

Step A: Fmoc-Gly Wang resin (20 g, 10.8 mmole, Novabiochem A16415) was reacted with a 30% solution of piperidine in N-methylpyrrolidinone (NMP) for 30 minutes. The solution was drained and the resin washed with NMP (5 x 200 mL). Benzophenone imine (19.5 g, 108 mmole) in NMP (150 mL) was added to the resin followed by glacial acetic acid (5.6 g, 94 mmole) and the reaction was mixed overnight at room temperature. Reagents were drained and the resin washed with NMP (5 x 150 mL) followed by DCM (5 x 150 mL). The resin was dried under vacuum to afford (benzophenone imine)-Gly Wang resin with a theoretical loading of 0.56 mmole per gram.

Step B: A suspension of the resin from Step A in NMP (9 mL) was reacted with an alkyl bromide (5.6 mL of 1 M solution in NMP) selected from 1-bromo-2-ethylbutane, 1-bromo-3-methylbutane, cyclopropylmethyl bromide, 1-bromo-2-cyclohexylethane, 1-bromo-4-fluorobutane, and 1-bromo-2-methylbutane; and BEMP (5.6 mL of 1 M solution in NMP) and Bu₄NI (5.6 mL of 1 M solution in NMP) for 20 hours at room temperature. Reagents were drained and the resin washed with NMP (3 x 15 mL). To a mixture of the resin in THF (7 mL) was added hydroxylamine hydrochloride (2 mL of a 1.6 M solution in water) and the reaction was mixed for 20 hours at room

temperature. Reagents were drained and the resin washed sequentially with THF (2 x 5 mL), 0.5 M solution of diisopropylethylamine in THF (5 mL), THF (5 mL), and NMP (3 x 5 mL).

5 Step C: The resin from Step B was divided into 12 equal reactions using
an isopicnic solution in NMP:CH₂Cl₂. To each reaction was added sequentially
a carboxylic acid (0.75 mL of a 0.45 M solution in NMP), HOBT (0.75 mL of
a 0.45 M solution in NMP) and DIC (0.75 mL of a 0.45 M solution in
NMP). The reaction was mixed for 18 hours at room temperature. Reagents
10 were drained and the resin washed with NMP (5 x 0.5 mL), and DCM (5 x 0.5
mL). The resin was mixed with TFA:H₂O (95:5, 0.5 mL) for 4 hours. The
filtrate was collected, resin washed with TFA:H₂O (95:5, 0.5 mL) and the
filtrates combined. Solvents were evaporated to yield the N-acyl amino acid.

GENERAL PROCEDURE C-R

Various acylated amino acids (approximately 0.02 mmole) (from General Procedure C-Q) in separate vials were reacted with 5-amino-7-methyl-5,7-dihydro-6H-dibenz[bd]azepin-6-one (0.1 mL, 0.3 M in DCM) (Example 7-A), PP-HOBT (0.2 mL, 0.15 M in DMF), and EDC-HCl (0.4 mL, 0.08 M in DCM). Reactions were mixed for 18 hours at room temperature. Reactions were diluted with 0.5 mL MeOH, loaded onto a Varian SCX column (500 mg, Varian Sample Preparations, pre-washed with MeOH (2.5 mL) and 10% MeOH:CHCl₃ (2.5 mL)), and eluted with 10% MeOH:CHCl₃ (2.5 mL). Solvents were evaporated from the products and the crude products purified by semi-prep reverse phase chromatography (gradient 0 to 100 %, 0.1% TFA in H₂O to 0.08% TFA in CH₃CN). The correct molecular ion was detected for each product by ionspray mass spec and analytical reverse phase chromatography (gradient 0 to 100 %, 0.01% TFA in H₂O to 0.08% TFA in CH₃CN) showed the products to be greater than 90% pure.

Using the procedures indicated, the compounds shown in Table C-4 were prepared. In this table, starting material 2 was prepared as described in Example 7-I.

Table C-4

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-1	5-{N'-(Cyclopentyl acetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	Cyclopentyl acetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	420.2
7C-2	5-{N'-(3-cyclopentylpropionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-cyclopentylpropionic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	434.2
7C-3	5-{N'-(cyclohexylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	cyclohexylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	434.2
7C-4	5-{N'-(t-butylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	t-butylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	408.2
7C-5	5-{N'-(phenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	phenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	428.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-6	5-{N'-(3-bromophenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-bromophenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	506.0, 508.0
7C-7	5-{N'-(3-fluorophenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-fluorophenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	446.0
7C-8	5-{N'-(3-chlorophenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-chlorophenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	462.2
7C-9	5-{N'-(3-(trifluoromethyl)phenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-(trifluoromethyl)phenylacetic acid (Marshallton)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	496.0
7C-10	5-{N'-(4-fluorophenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-fluorophenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	446.0
7C-11	5-{N'-(hexanoyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	hexanoic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	408.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-12	5-{N'-(heptanoyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	heptanoic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	422.2
7C-13	5-{3,4-difluorophenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3,4-difluorophenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	464.2
7C-14	5-{N'-(cyclopropylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	cyclopropylacetic acid (Lancaster)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	392.2
7C-15	5-{N'-(2-cyclopentene-1-acetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2-cyclopentene-1-acetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	418.2
7C-16	5-{N'-(3-cyclohexylpropionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-cyclohexylpropionic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	448.0
7C-17	5-{N'-(isovaleryl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	isovaleric acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	394.0

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-18	5-{N'-(citronellyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	citronellic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	462.2
7C-19	5-{N'-(3-benzoylpropionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-benzoylpropionic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	470.2
7C-20	5-{N'-(2-chlorophenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2-chlorophenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	462.2
7C-21	5-{N'-(4-pentenoyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-pentenoyl acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	392.0
7C-22	5-{N'-(valeryl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	valeric acid (Eastman)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	394.0
7C-23	5-{N'-(2-thiophenecetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2-thiophenecetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	434.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-24	5-{N'-(4-(2-thienyl)butyryl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-(2-thienyl)butyric acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	462.2
7C-25	5-{N'-(4-(4-nitrophenyl)butyryl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-(4-nitrophenyl)butyric acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	501.0
7C-26	5-{N'-(2,4-difluorophenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2,4-difluorophenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	464.2
7C-27	5-{N'-(2,6-difluorophenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2,6-difluorophenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	464.2
7C-28	5-{N'-(4-isopropylphenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-isopropylphenylacetic acid (Lancaster)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	470.2
7C-29	5-{N'-(1-adamantanecetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	1-adamantanecetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	486.4

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-30	5-{N'-(cyclohexanepentanoyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	cyclohexanepentanoic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	476.2
7C-31	5-{N'-(methylthioacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(methylthio)acetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	398.0
7C-32	5-{N'-(2-thiophenepentanoyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2-thiophenepentanoic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	476.0
7C-33	5-{N'-(2-norbornaneacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2-norbornaneacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	446.0
7C-34	5-{N'-(3,5-difluorophenylacetyl)-4-ethylnorleucinyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(3,5-difluorophenylacetyl)-4-ethylnorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[bd]azepin-6-one	C-R	534.2
7C-35	5-{N'-(3,5-difluorophenylacetyl)-4-methylnorleucinyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(3,5-difluorophenylacetyl)-4-methylnorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[bd]azepin-6-one	C-R	520.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-36	5-{N'-(3,5-difluorophenylacetyl)-3-cyclopropylalaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(3,5-difluorophenylacetyl)-3-cyclopropylalanine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[bd]azepin-6-one	C-R	504.0
7C-37	5-{N'-(3,5-difluorophenylacetyl)-4-cyclohexylthomoalaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(3,5-difluorophenylacetyl)-4-cyclohexylthomoalanine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[bd]azepin-6-one	C-R	560.2
7C-38	5-{N'-(3,5-difluorophenylacetyl)-6-fluoronorleucinyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(3,5-difluorophenylacetyl)-6-fluoronorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[bd]azepin-6-one	C-R	524.0
7C-39	5-{N'-(3,5-difluorophenylacetyl)-4-methylnorleucinyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(3,5-difluorophenylacetyl)-4-methylnorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[bd]azepin-6-one	C-R	520.0
7C-40	5-{N'-(cyclohexylacetyl)-4-ethylnorleucinyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(cyclohexylacetyl)-4-ethylnorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[bd]azepin-6-one	C-R	504.3
7C-41	5-{N'-(cyclopropylacetyl)-4-ethylnorleucinyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(cyclopropylacetyl)-4-ethylnorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[bd]azepin-6-one	C-R	462.3

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-42	5-{N'-(isovaleryl)-4-ethylnorleucinyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(isovaleryl)-4-ethylnorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[bd]azepin-6-one	C-R	464.3
7C-43	5-{N'-(3-(trifluoromethyl)phenylacetyl)-4-ethylnorleucinyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(3-(trifluoromethyl)phenylacetyl)-4-ethylnorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[bd]azepin-6-one	C-R	566.3
7C-44	5-{N'-(3,4-difluorophenylacetyl)-4-ethylnorleucinyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(3,4-difluorophenylacetyl)-4-ethylnorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[bd]azepin-6-one	C-R	534.3
7C-45	5-{N'-(2,4-difluorophenylacetyl)-4-ethylnorleucinyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(2,4-difluorophenylacetyl)-4-ethylnorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[bd]azepin-6-one	C-R	534.3
7C-46	5-{N'-(3-fluorophenylacetyl)-4-methylnorleucinyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(3-fluorophenylacetyl)-4-methylnorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[bd]azepin-6-one	C-R	502.3

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-47	5-{N'-(cyclopentylacetyl)-4-methylnorleucinyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(cyclopentylacetyl)-4-methylnorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[bd]azepin-6-one	C-R	476.3
7C-48	5-{N'-(cyclohexylacetyl)-4-methylnorleucinyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(cyclohexylacetyl)-4-methylnorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[bd]azepin-6-one	C-R	490.3
7C-49	5-{N'-(cyclopropylacetyl)-4-methylnorleucinyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(cyclopropylacetyl)-4-methylnorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[bd]azepin-6-one	C-R	448.2
7C-50	5-{N'-(2-thiopheneacetyl)-4-methylnorleucinyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(2-thiopheneacetyl)-4-methylnorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[bd]azepin-6-one	C-R	490.2
7C-51	5-{N'-(isovaleryl)-4-methylnorleucinyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(isovaleryl)-4-methylnorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[bd]azepin-6-one	C-R	450.3

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-52	5-{N'-(3-(trifluoromethyl)phenylacetyl)-4-methylnorleucyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(3-(trifluoromethyl)phenylacetyl)-4-methylnorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-R	552.3
7C-53	5-{N'-(4-fluorophenylacetyl)-4-methylnorleucyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(4-fluorophenylacetyl)-4-methylnorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-R	502.3
7C-54	5-{N'-(3,4-difluorophenylacetyl)-4-methylnorleucyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(3,4-difluorophenylacetyl)-4-methylnorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-R	520.2
7C-55	5-{N'-(2,4-difluorophenylacetyl)-4-methylnorleucyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(2,4-difluorophenylacetyl)-4-methylnorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-R	520.3
7C-56	5-{N'-(3-fluorophenylacetyl)-4-cyclohexylhomoalaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(3-fluorophenylacetyl)-4-cyclohexylhomoalanine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-R	542.3

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-57	5-{N'-(cyclopentylacetyl)-4-cyclohexylhomoalaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(cyclopentylacetyl)-4-cyclohexylhomoalanine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[bd]azepin-6-one	C-R	516.3
7C-58	5-{N'-(cyclohexylacetyl)-4-cyclohexylhomoalaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(cyclohexylacetyl)-4-cyclohexylhomoalanine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[bd]azepin-6-one	C-R	530.4
7C-59	5-{N'-(cyclopropylacetyl)-4-cyclohexylhomoalaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(cyclopropylacetyl)-4-cyclohexylhomoalanine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[bd]azepin-6-one	C-R	488.3
7C-60	5-{N'-(isovaleryl)-4-cyclohexylhomoalaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(isovaleryl)-4-cyclohexylhomoalanine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[bd]azepin-6-one	C-R	490.3
7C-61	5-{N'-(4-fluorophenylacetyl)-4-cyclohexylhomoalaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(4-fluorophenylacetyl)-4-cyclohexylhomoalanine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[bd]azepin-6-one	C-R	542.3
7C-62	5-{N'-(3,4-difluorophenylacetyl)-4-cyclohexylhomoalaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(3,4-difluorophenylacetyl)-4-cyclohexylhomoalanine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[bd]azepin-6-one	C-R	560.3

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-63	5-{N'-(2,4-difluorophenylacetyl)-4-cyclohexylhomoalaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(2,4-difluorophenylacetyl)-4-cyclohexylhomoalanine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-R	560.3
7C-64	5-{N'-(3-fluorophenylacetyl)-6-fluoronorleucinyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(3-fluorophenylacetyl)-6-fluoronorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-R	506.2
7C-65	5-{N'-(cyclopentylacetyl)-6-fluoronorleucinyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(cyclopentylacetyl)-6-fluoronorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-R	480.3
7C-66	5-{N'-(cyclohexylacetyl)-6-fluoronorleucinyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(cyclohexylacetyl)-6-fluoronorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-R	494.3
7C-67	5-{N'-(cyclopropylacetyl)-6-fluoronorleucinyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(cyclopropylacetyl)-6-fluoronorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-R	452.2
7C-68	5-{N'-(isovaleryl)-6-fluoronorleucinyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(isovaleryl)-6-fluoronorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-R	454.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-69	5-{N'-(3-(trifluoromethyl)phenylacetyl)-6-fluoronorleucyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(3-(trifluoromethyl)phenylacetyl)-6-fluoronorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-R	556.2
7C-70	5-{N'-(4-fluorophenylacetyl)-6-fluoronorleucyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(4-fluorophenylacetyl)-6-fluoronorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-R	506.2
7C-71	5-{N'-(3,4-difluorophenylacetyl)-6-fluoronorleucyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(3,4-difluorophenylacetyl)-6-fluoronorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-R	524.2
7C-72	5-{N'-(2,4-difluorophenylacetyl)-6-fluoronorleucyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(2,4-difluorophenylacetyl)-6-fluoronorleucine (General Procedure C-Q)	5-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-R	524.2
7C-73	5-{N'-(4-methoxyphenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-methoxyphenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	458.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-74	5-{N'-(3-(4-methoxyphenyl)propionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-(4-methoxyphenyl)propionic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	472.2
7C-75	5-{N'-(1-naphthylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	1-naphthylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	478.2
7C-76	5-{N'-(3,4-methylenedioxyphenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3,4-methylenedioxyphenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	472.2
7C-77	5-{N'-(hydrocinnamyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	hydrocinnamic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	442.2
7C-78	5-{N'-(octanoyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	octanoic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	436.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-79	5-{N'-(3-(3-hydroxyphenyl)propionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-(3-hydroxyphenyl)propionic acid (Lancaster)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	458.2
7C-80	5-{N'-(3-(4-methylphenyl)propionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-(4-methylphenyl)propionic acid (Lancaster)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	456.2
7C-81	5-{N'-(3-(4-chlorophenyl)propionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-(4-chlorophenyl)propionic acid (Trans World)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	476.1, 478.1
7C-82	5-{N'-(3-phenylbutyryl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-phenylbutyric acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	456.2
7C-83	5-{N'-(3-(4-hydroxyphenyl)propionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-(4-hydroxyphenyl)propionic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	458.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-84	5-{N'-(3,4,5-trifluorophenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3,4,5-trifluorophenylacetic acid (Fluorochem)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	482.1
7C-85	5-{N'-(4-(4-methoxyphenyl)butyryl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-(4-methoxyphenyl)butyric acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	486.2
7C-86	5-{N'-(3-(Methoxycarbonyl)propionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	mono-methyl succinate = 3-(Methoxycarbonyl)propionic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	424.1
7C-87	5-{N'-(4-phenylbutyryl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-phenylbutyric acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	456.2
7C-88	5-{N'-(3-(benzylthio)propionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-(benzylthio)propionic acid (Sigma-Aldrich Rare)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	488.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-89	5-{N'-(3-methylpentanoyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-methylpentanoic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	408.2
7C-90	5-{N'-(7-carbomethoxyheptanoyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	suberic acid monomethyl ester = 7-carbomethoxyheptanoic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	480.2
7C-91	5-{N'-(2-indanylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2-indanylacetic acid (Lancaster)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	468.2
7C-92	5-{N'-(5-Carbomethoxypentanoyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	monomethyl adipate = 5-Carbomethoxypentanoic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	452.2
7C-93	5-{N'-(2-methyl-3-Benzofuranacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2-methyl-3-Benzofuranacetic acid (Maybridge)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	482.2
7C-94	5-{N'-(propionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	propionic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	366.1

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-95	5-{N'-(3-methoxypropionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-methoxypropionic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	396.1
7C-96	5-{N'-(3-(4-fluorophenyl)propionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-(4-fluorophenyl)propionic acid (Trans World)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	460.2
7C-97	5-{N'-(3-(4-fluorophenoxy)propionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-(4-fluorophenoxy)propionic acid (Maybridge)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	476.1
7C-98	5-{N'-(4-toluenesulfonylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-toluenesulfonylacetic acid (Lancaster)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	506.1
7C-99	5-{N'-(3-pentenoyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-pentenoyl acid (Fluka)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	392.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-100	5-{N'-(4-(2,4-dichlorophenoxy)butyryl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-(2,4-dichlorophenoxy)butyric acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	540.1, 542.1
7C-101	5-{N'-(2,3-dichlorophenoxyacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2,3-dichlorophenoxyacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	512.1, 514.1
7C-102	5-{N'-(3-(4-chlorobenzoyl)propionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-(4-chlorobenzoyl)propionic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	504.1, 506.1
7C-103	5-{N'-(4'-fluorosuccinanylyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4'-fluorosuccinanylic acid (Sigma-Aldrich Rare)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	503.2
7C-104	5-{N'-(n-(diphenylmethyl)glutaramyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	n-(diphenylmethyl)glutaramic acid (Sigma-Aldrich Rare)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	589.3

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-105	5-{N'-(2-fluorophenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2-fluorophenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	446.2
7C-106	5-{N'-(cyanoacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	cyanoacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	377.1
7C-107	5-{N'-(succinanilyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	succinanilic acid (Sigma-Aldrich Rare)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	485.2
7C-108	5-{N'-(2,4-dichlorophenoxyacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2,4-dichlorophenoxyacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	512.1, 514.1
7C-109	5-{N'-(2-nitrophenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2-nitrophenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	473.2
7C-110	5-{N'-(beta-propylhydrocinnamyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	beta-propylhydrocinnamic acid (Sigma-Aldrich Rare)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	484.3

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-111	5-{N'-(3-(2,4-dimethylbenzoyl)propionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-(2,4-dimethylbenzoyl)propionic acid (Sigma-Aldrich Rare)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	498.2
7C-112	5-{N'-(2-fluoro-3-(trifluoromethyl)phenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2-fluoro-3-(trifluoromethyl)phenylacetic acid (Fluorochem)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	514.3
7C-113	5-{N'-(2,4,6-trifluorophenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2,4,6-trifluorophenylacetic acid (Fluorochem)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	482.2
7C-114	5-{N'-(4-fluoro-2-(trifluoromethyl)phenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-fluoro-2-(trifluoromethyl)phenylacetic acid (Fluorochem)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	514.2
7C-115	5-{N'-(2-fluoro-4-(trifluoromethyl)phenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2-fluoro-4-(trifluoromethyl)phenylacetic acid (Fluorochem)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	514.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-116	5-{N'-(4-hydroxyphenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-hydroxyphenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	444.2
7C-117	5-{N'-(4-methoxyphenoxyacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-methoxyphenoxyacetic acid (Lancaster)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	474.2
7C-118	5-{N'-(2-methoxyphenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2-methoxyphenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	458.2
7C-119	5-{N'-(2-bromophenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2-bromophenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	508.1
7C-120	5-{N'-(4-benzyloxyphenoxyacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-benzyloxyphenoxyacetic acid (Lancaster)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	550.2
7C-121	5-{N'-(4-hydroxyphenoxyacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-hydroxyphenoxyacetic acid (Acros)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	460.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-122	5-{N'-(levuliny)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	levulinic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	408.2
7C-123	5-{N'-(2-hydroxyphenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2-hydroxyphenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	444.2
7C-124	5-{N'-(3,4-dimethoxyphenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3,4-dimethoxyphenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	488.2
7C-125	5-{N'-(3-(4-methoxybenzoyl)propionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-(4-methoxybenzoyl)propionic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	500.2
7C-126	5-{N'-(3-(4-Phenylbenzoyl)propionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	fenbufen = 3-(4-Phenylbenzoyl)propionic acid (Sigma-Aldrich Rare)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	546.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-127	5-{N'-(3-hydroxyphenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-hydroxyphenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	444.2
7C-128	5-{N'-(N-acetyl-N-phenylglycyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	N-acetyl-N-phenylglycine (Kodak)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	485.2
7C-129	5-{N'-(thiophene-3-acetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	thiophene-3-acetic acid. (Acros)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	434.1
7C-130	5-{N'-(6-phenylhexanoyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	6-phenylhexanoic acid (Avocado)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	484.3
7C-131	5-{N'-(cyclohexanebutyryl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	cyclohexanebutyric acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	462.3
7C-132	5-{N'-(2,3,5-trifluorophenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2,3,5-trifluorophenylacetic acid (Fluorochem)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	482.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-133	5-{N'-(2,4,5-trifluorophenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2,4,5-trifluorophenylacetic acid (Fluorochem)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	482.2
7C-134	5-{N'-(vinylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	vinylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	378.2
7C-135	5-{N'-(3-methylthiopropionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-methylthiopropionic acid (Lancaster)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	412.1
7C-136	5-{N'-(3-nitrophenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-nitrophenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	473.2
7C-137	5-{N'-(n-tert-butylsuccinamyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	n-tert-butylsuccinamic acid (Sigma-Aldrich Rare)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	465.2
7C-138	5-{N'-(4-bromophenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-bromophenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	506.1, 508.1

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-139	5-{N'-(3-(4-fluorobenzoyl)propionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-(4-fluorobenzoyl)propionic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	488.2
7C-140	5-{N'-(o-chlorophenoxyacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	o-chlorophenoxyacetic acid (Lancaster)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	478.1, 480.1
7C-141	5-{N'-(p-tolylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	p-tolylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	442.2
7C-142	5-{N'-(m-tolylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	m-tolylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	442.2
7C-143	5-{N'-(3,4-dichlorophenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3,4-dichlorophenylacetic acid (Fairfield)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	496.1, 498.1
7C-144	5-{N'-(4-chlorophenoxyacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-chlorophenoxyacetic acid (Grand Island Biological)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	478.1, 480.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-145	5-{N'-(3-methylphenoxyacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-methylphenoxyacetic acid (Lancaster)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	458.2
7C-146	5-{N'-(4-isopropylphenoxyacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-isopropylphenoxyacetic acid (Lancaster)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	486.2
7C-147	5-{N'-(4-phenoxyphenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-phenoxyphenylacetic acid (Trans World)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	520.2
7C-148	5-{N'-(phenylmercaptoacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	phenylmercaptoacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	460.2
7C-149	5-{N'-(4-ethoxyphenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-ethoxyphenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	472.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-150	5-{N'-(2,5-dimethoxyphenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2,5-dimethoxyphenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	488.2
7C-151	5-{N'-(o-tolylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	o-tolylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	442.2
7C-152	5-{N'-(3,3-diphenylpropionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3,3-diphenylpropionic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	518.2
7C-153	5-{N'-(3-phenoxypropionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-phenoxypropionic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	458.2
7C-154	5-{N'-(4-(trifluoromethyl)phenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-(trifluoromethyl)phenylacetic acid (Maybridge)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	496.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-155	5-{N'-(4-methylphenoxy)acetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(4-methylphenoxy)acetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	458.2
7C-156	5-{N'-(2-phenoxyphenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2-phenoxyphenylacetic acid (Trans World)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	520.2
7C-157	5-{N'-(3-phenoxyphenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-phenoxyphenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	520.2
7C-158	5-{N'-(3,4-dichlorophenoxyacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3,4-dichlorophenoxyacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	512.1, 514.1
7C-159	5-{N'-(4-fluorophenoxyacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-fluorophenoxyacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	462.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-160	5-{N'-(3,4,5-trimethoxyphenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3,4,5-trimethoxyphenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	518.2
7C-161	5-{N'-(2,4-dichlorophenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2,4-dichlorophenylacetic acid (Fairfield)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	496.1, 498.1
7C-162	5-{N'-(4-thianaphthenacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-thianaphthenacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	484.2
7C-163	5-{N'-(methoxyacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	methoxyacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	382.2
7C-164	5-{N'-(ethoxyacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	ethoxyacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	396.2
7C-165	5-{N'-(phenoxyacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	phenoxyacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	444.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-166	5-{N'-(3-methoxyphenoxyacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-methoxyphenoxyacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	474.2
7C-167	5-{N'-(4-butoxyphenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-butoxyphenylacetic acid (Lancaster)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	500.3
7C-168	5-{N'-(3-(2-methoxyphenyl)propionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-(2-methoxyphenyl)propionic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	472.2
7C-169	5-{N'-(N,N-dimethylsuccinamyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	N,N-dimethylsuccinamic acid (Lancaster)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	437.2
7C-170	5-{N'-(3-(3,4-methylenedioxyphenyl)propionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-(3,4-methylenedioxyphenyl)propionic acid (Lilly)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	486.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-171	5-{N'-(2-Chloro-6-fluorophenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2-Chloro-6-fluorophenylacetic acid	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	480.1, 482.1
7C-172	5-{N'-(2,5-difluorophenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2,5-difluorophenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	464.2
7C-173	5-{N'-(pentafluorophenoxyacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	pentafluorophenoxyacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	534.2
7C-174	5-{N'-(3,5-bis(trifluoromethyl)phenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3,5-bis(trifluoromethyl)phenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	564.2
7C-175	5-{N'-(3,5-dimethylphenoxyacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3,5-dimethylphenoxyacetic acid (Sigma-Aldrich Rare)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	472.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-176	5-{N'-(4-chlorophenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-chlorophenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	462.1, 464.1
7C-177	5-{N'-(3-chlorophenoxyacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-chlorophenoxyacetic acid (Lancaster)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	478.1, 480.2
7C-178	5-{N'-(benzo [b] thiophene-3-acetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	benzo [b] thiophene-3-acetic acid (Lancaster)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	484.2
7C-179	5-{N'-(3,5-dimethoxyphenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3,5-dimethoxyphenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	488.2
7C-180	5-{N'-(2,5-dimethylphenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2,5-dimethylphenylacetic acid (Lancaster)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	456.2
7C-181	5-{N'-(mesitylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	mesitylacetic acid (Lancaster)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	470.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-182	5-{N'-(4-biphenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-biphenylacetic acid (Lancaster)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	504.2
7C-183	5-{N'-(N-(tert-butoxycarbonyl)-3-aminopropionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	boc-beta-ala-oh = N-(tert-butoxycarbonyl)-3-aminopropionic acid (Sigma)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	381.2, 481.2
7C-184	5-{N'-(trans-styrylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	trans-styrylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	454.2
7C-185	5-{N'-(4-acetamidobutyryl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-acetamidobutyric acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	437.2
7C-186	5-{N'-(3-(2-chlorophenyl)propionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-(2-chlorophenyl)propionic acid (Trans World)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	476.2, 478.2
7C-187	5-{N'-(butyryl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	butyric acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	380.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-188	5-{N'-(trans-3-hexenyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	trans-3-hexenoic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	406.2
7C-189	5-{N'-(5-phenylvaleryl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	5-phenylvaleric acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	470.2
7C-190	5-{N'-(3-(3-methoxyphenyl)propionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-(3-methoxyphenyl)propionic acid (Lancaster)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	472.2
7C-191	5-{N'-(4-chloro-beta-methylhydrocinnamyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-chloro-beta-methylhydrocinnamic acid (Sigma-Aldrich Rare)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	490.2, 492.2
7C-192	5-{N'-(3-(trifluoromethyl)butyryl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-(trifluoromethyl)butyric acid (Fluorochem)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	448.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-193	5-{N'-(methanesulfonylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	methanesulfonylacetic acid (Lancaster)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	430.1
7C-194	5-{N'-(alpha-naphthoxyacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	alpha-naphthoxyacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	494.2
7C-195	5-{N'-(3-(4-phenoxybenzoyl)propionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-(4-phenoxybenzoyl)propionic acid (Sigma-Aldrich Rare)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	562.2
7C-196	5-{N'-(3-(2-trifluoromethylbenzoyl)propionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-(2-trifluoromethylbenzoyl)propionic acid (Sigma-Aldrich Rare)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	538.2
7C-197	5-{N'-(3-benzoylamino-3-phenylpropionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-benzoylamino-3-phenylpropionic acid (Sigma-Aldrich Rare)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	561.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-198	5-{N'-(4-(hydroxyimino)pentanoyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	levulinic acid oxime = 4-(hydroxyimino)pentanoic acid (Sigma-Aldrich Rare)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	423.2
7C-199	5-{N'-(4'-methylglutaranilyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4'-methylglutaranilic acid (Sigma-Aldrich Rare)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	499.2
7C-200	5-{N'-(4-(4-ethyl-phenoxy)-phenoxy)-acetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(4-(4-ethyl-phenoxy)-phenoxy)-acetic acid (Sigma-Aldrich Rare)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	564.2
7C-201	5-{N'-(3-Benzoyl-3-phenylpropionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-Benzoyl-3-phenylpropionic acid (Sigma-Aldrich Rare)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	528.2, 546.2
7C-202	5-{N'-(4-(hydroxymethyl)phenoxyacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-(hydroxymethyl)phenoxyacetic acid (Sigma)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	456.2, 474.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-203	5-{N'-(4,4,4-trifluorobutyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4,4,4-trifluorobutyric acid (Fluorochem)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	434.1
7C-204	5-{N'-(3-isobutyrylamino-3-phenylpropionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-isobutyrylamino-3-phenylpropionic acid (Sigma-Aldrich Rare)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	527.3
7C-205	5-{N'-(2-methylphenoxyacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	(2-methylphenoxy)acetic acid (Lancaster)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	458.2
7C-206	5-{N'-(3-(phenylsulfonyl)propionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-(phenylsulfonyl)propionic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	506.2
7C-207	5-{N'-(4-nitrophenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-nitrophenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	473.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-208	5-{N'-(3-ethoxypropionyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3-ethoxypropionic acid (TCI)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	410.2
7C-209	5-{N'-(2,3-difluoromandelyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2,3-difluoromandelic acid (Fluorochem)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	480.2
7C-210	5-{N'-(2,6-difluoromandelyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2,6-difluoromandelic acid (Fluorochem)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	480.2
7C-211	5-{N'-(4-fluoromandelyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-fluoromandelic acid (Lancaster)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	462.2
7C-212	5-{N'-(2,5-difluoromandelyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2,5-difluoromandelic acid (Fluorochem)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	480.2
7C-213	5-{N'-(dl-beta-phenyllactyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	dl-beta-phenyllactic acid (Sigma)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	458.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-214	5-{N'-(dl-mandelyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	dl-mandelic acid or dl-alpha-hydroxyphenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	444.2
7C-215	5-{N'-(p-chloromandelyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	p-chloromandelic acid (Acros)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	444.2, 478.1
7C-216	5-{N'-(l-alpha-hydroxyisocaproyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	l-alpha-hydroxyisocaproic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	424.2
7C-217	5-{N'-(4-bromomandelyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-bromomandelic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	522.1, 524.1
7C-218	5-{N'-(l-(+)-lactyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	l-(+)-lactic acid (Sigma)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	382.2, 454.2
7C-219	5-{N'-(d-3-phenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	d-3-phenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	458.2

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-220	5-{N'-(5-methylhexanoyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	5-methylhexanoic acid (P&B)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	422.2

GENERAL PROCEDURE C-S

Step A: Each amino acid (150 μmol) was weighed into an 8-mL capacity vial and dissolved in 1.5 mL of 10% DMF in dichloromethane (DCM). To each vial was added 0.8 mL (175 μmol) of a solution of 5-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one hydrochloride (481 mg, 1.75 mmol) (from Example 7-A) and 670 mg (1.75 mmol) of PP-HOBT (from Example C-AF) dissolved in 7.5 mL DMF. This was followed by the addition to each vial of 2 mL (approximately 200 μmol) of a solution of EDC hydrochloride in DCM (383 mg, 2.0 mmol in 20 mL DCM). After rocking the vials at room temperature for 14 hours, approximately 100-125 mg of polystyrene-piperidine resin (approximately 3.6 mmol/g, 350 μmol , 2.33 eq.) was added to each vial and rocking continued for 15 minutes. Methanol (2.5 mL) was added to each vial and the material put on a 1 g SCX column (Varian) pre-equilibrated with 5 mL of MeOH and 5 mL of 10% MeOH/chloroform. After pushing the liquid through the column with nitrogen, the column was washed with 5 mL of 10% MeOH/chloroform. The combined eluants (collected in 25 mL roundbottom flasks) were evaporated at reduced pressure with a warm water bath at 30-35°C and then further evaporated in a vacuum oven at 40-45°C. When the net weight of the residues was below 100 mg, 5 mL of dioxane and, if necessary, 1 mL of MeOH was added to redissolve the residue and solvent was again removed on the rotary evaporator and in the vacuum oven. After drying in the vacuum oven overnight, an HPLC was taken of each product. HPLC show primarily the desired product and with about 15% deblocked product (i.e., product with the BOC group removed).

25

Step B: To each round bottom flask was added 5 mL of 4 N HCl in dioxane. After sitting at room temperature for 2-3 hours, an HPLC was taken and was solvent removed on the rotary evaporator (bath temp 30-35°C) and in the vacuum oven overnight (at approximately 40°C). The HPLC of the t-butyl threonine adduct showed incomplete removal of the t-butyl group. An additional 5 mL of 4 N HCl in dioxane was added and the reaction (at room

30

temperature) monitored by HPLC at 4 hours and approximately 20 hours. Complete removal of the t-butyl group was observed after 20 hours. All products were pure by HPLC with only a single peak or resolved diastereomeric peaks observed except for some trace impurities in the methione case. Yields varied from 80 to 100%. Each round bottom contained approximately 150 umoles of the amino acid linked to 5-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one.

Step C: A stock solution of 567 mg (1.48 mmol) PP-HOBT in 8.5 mL DMF (approximately 0.175 M PP-HOBT in DMF) was prepared and 0.81 g (0.86 mL, 150 umol) of this PP-HOBT solution was added to each of the nine round-bottom vessels containing the products from Step B. Clear solutions were obtained for all, except where the linked amino acid was alpha amino isobutyric acid. In this case, an additional 0.86 mL of DMF was added but still the mixture remained heterogeneous. The contents of each of the nine round bottoms "n" (where n = 1 to 9) were divided into four equal portions (approximately 37 umols each) and placed in vials. Stock solutions (0.1 M) of the carboxylic acids were then made up in 10% DMF/DCM. The appropriate stock solution (0.3 mL, 30 umol) was then added to each of the vials. A 0.1 M stock solution (20 mL) of EDC hydrochloride in DMF was prepared. This stock solution (0.4 mL, 40 umol) was then added to each of the vials which were then capped and put on a rotator for 12 hours. Normal SCX workup and evaporation of solvent afforded products as white solids or clear to light caramel resins. Each of these products was taken up in methanol/chloroform and divided into three tared vials, plus a vial for MS and HPLC characterization. After evaporation of solvent, the final weights in each vial were determined. Product identity was verified by ionspray mass spec and purity assessed by reverse phase HPLC.

Example C-AF

Preparation of PP-HOBT

To a stirred solution of 7.68g (30 mmol) sulfonyl chloride in 120 mL of dichloromethane was added dropwise, over a 10 min period, 5.04g (30 mmol) of 4-piperidino-piperidine (Aldrich, 90%) and 3.6 g (36 mmol) of triethylamine in 30 mL of dichloromethane. A mildly exothermic reaction ensued. After stirring 2 hours at room temperature, the orange solution was diluted with 100 mL of dichloromethane and washed with 10% sodium bicarbonate solution (2 x 100 mL) and brine (1 x 100 mL). After drying over sodium sulfate, the solvent was removed at reduced pressure to afford 10.7 g of crude product as a light tan solid ($R_f = 0.5$, Silica, 10% MeOH/chloroform).

To this crude material was added 200 mL of 95% EtOH/5% MeOH followed by 60 mL of hydrazine hydrate. The mixture was refluxed for 3 hours. During the first 0.5 hour, the initially orange solution turned deep red-orange before turning orange again. After refluxing for 3 hours, most of the solvent, water and hydrazine was removed at reduced pressure. To the residue was added 50 mL of EtOH and solvent removed at reduced pressure. This was repeated 2 or more times to give a tan solid which was further dried in the vacuum oven to a constant weight of 13.5 g. To the flask containing this solid was added 250 mL of water. Almost all of the solid went into solution, then a fine light yellow precipitate formed. After stirring cooled in an ice bath for two hours, the solid was collected by vacuum filtration through a sintered glass filter, and rinsed with about 20 mL of cold water. Drying in the vacuum oven at 40°C overnight afforded 7.3 g (63% yield) of the title compound (PP-HOBT) as an off-white crunchy powder, mp 195-200°C (dec).

Using the procedures indicated, the compounds shown in Table C-5 were prepared. Starting material 2 used in these procedures was prepared as described in General Procedure C-S.

Table C-5

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-221	5-{N'-(3,5-difluorophenylacetyl)-L-methioninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3,5-difluorophenylacetic acid (Aldrich)	5-(L-methioninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-S	524.3
7C-222	5-{N'-(3,5-difluorophenylacetyl)-L-2-phenylglycinyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3,5-difluorophenylacetic acid (Aldrich)	5-(L-2-phenylglycinyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-S	526.5
7C-223	5-{N'-(3,5-difluorophenylacetyl)-L-leucinyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3,5-difluorophenylacetic acid (Aldrich)	5-(L-leucinyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-S	506.3
7C-224	5-{N'-(3,5-difluorophenylacetyl)-L-2-cyclohexylglycinyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3,5-difluorophenylacetic acid (Aldrich)	5-(L-2-cyclohexylglycinyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-S	532.3
7C-225	5-{N'-(3,5-difluorophenylacetyl)-L-threoninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3,5-difluorophenylacetic acid (Aldrich)	5-(L-threoninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-S	494.5

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-226	5-{N'-(3,5-difluorophenylacetyl)-L-alpha-(2-thienyl)glycyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	3,5-difluorophenylacetic acid (Aldrich)	5-(L-alpha-(2-thienyl)glycyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-S	532.2
7C-227	5-{N'-(2-thiopheneacetyl)-L-methioninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2-thiopheneacetic acid (Aldrich)	5-(L-methioninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-S	494.3
7C-228	5-{N'-(2-thiopheneacetyl)-L-2-phenylglycyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2-thiopheneacetic acid (Aldrich)	5-(L-2-phenylglycyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-S	496.2
7C-229	5-{N'-(2-thiopheneacetyl)-L-leucyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2-thiopheneacetic acid (Aldrich)	5-(L-leucyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-S	476.2
7C-230	5-{N'-(2-thiopheneacetyl)-L-2-cyclohexylglycyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2-thiopheneacetic acid (Aldrich)	5-(L-2-cyclohexylglycyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-S	502.2
7C-231	5-{N'-(2-thiopheneacetyl)-L-threoninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2-thiopheneacetic acid (Aldrich)	5-(L-threoninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-S	464.3

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-232	5-{N'-(2-thiopheneacetyl)-L-alpha-(2-thienyl)glycyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	2-thiopheneacetic acid (Aldrich)	5-(L-alpha-(2-thienyl)glycyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-S	502.1
7C-233	5-{N'-(isovaleryl)-L-methionyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	isovaleric acid (Aldrich)	5-(L-methionyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-S	454.2
7C-234	5-{N'-(isovaleryl)-L-2-phenylglycyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	isovaleric acid (Aldrich)	5-(L-2-phenylglycyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-S	456.4
7C-235	5-{N'-(isovaleryl)-L-leucyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	isovaleric acid (Aldrich)	5-(L-leucyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-S	436.4
7C-236	5-{N'-(isovaleryl)-L-2-cyclohexylglycyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	isovaleric acid (Aldrich)	5-(L-2-cyclohexylglycyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-S	462.6
7C-237	5-{N'-(isovaleryl)-L-threonyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	isovaleric acid (Aldrich)	5-(L-threoninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-S	424.3

Example No.	Compound	Starting Material I	Starting Material 2	General Procedure	MS
7C-238	5-{N'-(isovaleryl)-L-alpha-(2-thienyl)glycyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	isovaleric acid (Aldrich)	5-(L-alpha-(2-thienyl)glycyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-S	462.3
7C-239	5-{N'-(phenylacetyl)-L-methionyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	phenylacetic acid (Aldrich)	5-(L-methionyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-S	488.5
7C-240	5-{N'-(phenylacetyl)-L-2-phenylglycyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	phenylacetic acid (Aldrich)	5-(L-2-phenylglycyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-S	490.6
7C-241	5-{N'-(phenylacetyl)-L-leucyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	phenylacetic acid (Aldrich)	5-(L-leucyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-S	470.4
7C-242	5-{N'-(phenylacetyl)-L-2-cyclohexylglycyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	phenylacetic acid (Aldrich)	5-(L-2-cyclohexylglycyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-S	496.3
7C-243	5-{N'-(phenylacetyl)-L-threoninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	phenylacetic acid (Aldrich)	5-(L-threoninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-S	458.5

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-244	5-{N'-(phenylacetyl)-L-alpha-(2-thienyl)glycinyI}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	phenylacetic acid (Aldrich)	5-(L-alpha-(2-thienyl)glycinyI)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-S	496.2

Additionally, the following procedures provide various carboxylic acid esters which can be hydrolyzed using General Procedures AC or BD below to afford the corresponding carboxylic acids. Coupling of the resulting carboxylic acids to the amines employed above using the General Procedures set forth
5 above provides for additional compounds within the scope of this invention.

GENERAL PROCEDURE AA

Reductive Amination

10 To a solution of the arylamine in ethanol in a hydrogenation flask was added 1 equivalent of the 2-oxocarboxylic acid ester (e.g., pyruvate ester), followed by 10% palladium on carbon (25 weight percent based on the arylamine). The reaction was hydrogenated at 20 psi H₂ on a Parr shaker until complete reaction was indicated by tlc (30 minutes to 16 hours). The reaction
15 mixture was then filtered through a pad of Celite 545 (available from Aldrich Chemical Company, Inc.) and stripped free of solvent on a rotary evaporator. The crude product residue was then further purified via chromatography.

GENERAL PROCEDURE AB

First Transesterification Technique

20 A solution of 1-5 equivalents of the desired alcohol was added to 1 equivalent of sodium hydride in toluene. After off-gassing had ceased, the compound to be transesterified, dissolved in toluene, was added. After 0.5 hours, the reaction was either heated to 40°C and placed under house vacuum (~ 20 mmHg), or nitrogen was bubbled through the solution while it was heated
25 at 90°C. The reaction was followed by tlc, and when the reaction was complete the solution was cooled and quenched with water or 1M HCl, and in smaller scale reactions diluted with ethyl acetate. The organic phase was extracted with saturated aqueous NaHCO₃, then washed with saturated aqueous
30 NaCl and dried over MgSO₄. The solution was stripped free of solvent on a rotary evaporator, and the crude product residue was then further purified by

chromatography. Alternatively, the reaction mixture was worked-up by evaporation of the solvents and direct chromatography of the crude mixture.

5 This procedure is particularly useful in the case of costly and/or high boiling alcohols.

GENERAL PROCEDURE AC

Second Transesterification Technique

10 The compound to be transesterified was placed in a large excess of the desired alcohol. A catalytic amount of dry NaH was added, and the reaction was followed by tlc until the presence of starting material was no longer detected. The reaction was quenched with a few milliliters of 1N HCl, and after a few minutes of stirring saturated aqueous NaHCO₃ was added. The organic phase was washed with saturated aqueous NaCl and dried over MgSO₄. The
15 solution was stripped free of solvent on a rotary evaporator, and the crude product residue was then further purified by chromatography.

GENERAL PROCEDURE AD

Third Transesterification Technique

20 The compound to be transesterified was placed in a large excess of the desired alcohol. A catalytic amount of dry NaH was added, and the reaction was followed by tlc until the presence of starting material was no longer detected. The reaction was quenched with a few milliliters of 1N HCl, and after a few minutes of stirring saturated aqueous NaHCO₃ was added. The
25 volume of the reaction mixture was reduced on a rotary evaporator until the excess alcohol was removed and then the remaining residue was taken up in ethyl acetate and additional water was added. The organic phase was washed with saturated aqueous NaCl and dried over MgSO₄. The solution was stripped free of solvent on a rotary evaporator, and the crude product residue was then
30 further purified by chromatography.

This procedure is particularly employed in the case of low boiling, inexpensive alcohols, miscible with water.

GENERAL PROCEDURE AE

5

O-Alkylation Technique

To a carboxylic acid compound (prepared, for example, by reductive amination via General Procedure AA to provide for the *N*-aryl amino acid ester, followed by hydrolysis via Procedure AF) in DMF was added 1.5 equivalents K_2CO_3 , followed by 1 equivalent of alkylating agent (e.g., *tert*-butyl bromoacetate). The reaction was stirred at room temperature for 2 hours, then was quenched with water and extracted into ethyl acetate. The organic phase was washed with saturated aqueous $NaHCO_3$, water, and saturated aqueous $NaCl$, and was then dried over $MgSO_4$. The solution was stripped free of solvent on a rotary evaporator to yield the crude product.

15

GENERAL PROCEDURE AF

Ester Hydrolysis to Free Acid

To a carboxylic ester compound (prepared, for example, by reductive amination via General Procedure AA to provide for the *N*-aryl amino acid ester) in a 1:1 mixture of CH_3OH/H_2O was added 2-5 equivalents of K_2CO_3 . The mixture was heated to $50^\circ C$ for 0.5 to 1.5 hours until tlc showed complete reaction. The reaction was cooled to room temperature and the methanol was removed on a rotary evaporator. The pH of the remaining aqueous solution was adjusted to ~ 2 , and ethyl acetate was added to extract the product. The organic phase was then washed with saturated aqueous $NaCl$ and dried over $MgSO_4$. The solution was stripped free of solvent on a rotary evaporator to yield the crude product.

25

GENERAL PROCEDURE AG

30

N-Heteroarylation of Alanine

A solution of 1.1 equivalents of L-alanine and 2 equivalents NaOH in DMSO was stirred at room temperature for 1 hour, then 1 equivalent of 2-chlorobenzothiazole was added. The mixture was heated to 100°C for 4 hours, then cooled to room temperature and poured onto ice. The pH of the resulting aqueous solution was adjusted to ~2, and the precipitated solid was removed by filtration. This solid was then dissolved in 1N NaOH and the resulting solution was filtered through a pad of Celite 545. The pH of the filtrate was adjusted to ~2, and the white precipitate was removed by filtration and washed with water to yield the crude product.

GENERAL PROCEDURE AH

EDC Coupling

To a 1:1 mixture of the desired acid and alcohol in CH_2Cl_2 at 0°C was added 1.5 equivalents triethylamine, followed by 2.0 equivalents hydroxybenzotriazole monohydrate, then 1.25 equivalents of ethyl-3-(3-dimethylamino)-propyl carbodiimide·HCl (EDC). The reaction was stirred overnight at room temperature, then transferred to a separatory funnel and washed with water, saturated aqueous NaHCO_3 , 1N HCl, and saturated aqueous NaCl, and was then dried over MgSO_4 . The solution was stripped free of solvent on a rotary evaporator to yield the crude product.

GENERAL PROCEDURE AI

Oxime or Amine Coupling Technique

The trichlorophenyl ester (1 eq) of a carboxylic acid was stirred in DMF or THF. The oxime or amine (1.2 eq) was added and the mixture was stirred at ambient temperature for 1-4 hours. In cases where the hydrochloride salt form of an amine was used, a suitable base such as *N,N*-diisopropylethylamine (1.2 eq) was also added. The resulting mixture was concentrated under reduced pressure to yield a crude product which was used without purification or was purified by silica gel chromatography and/or crystallization.

GENERAL PROCEDURE AJ

Alkylation Technique

5 The amine (1 eq), the α -bromo ester (1.1 eq) and a suitable base (such as triethylamine) (2 eq) were stirred in chloroform. The resulting solution was heated at reflux for 4-12 hours. After cooling, the mixture was diluted with chloroform and washed with water. The organic portion was dried (sodium sulfate) and concentrated under reduced pressure. The crude product was purified by silica gel chromatography.

10 GENERAL PROCEDURE AK

Oxime or Alcohol Coupling Technique

The carboxylic acid (1 eq) was stirred in a suitable solvent (such as THF, dioxane or DMF). An alcohol or oxime (1-5 eq) was added. EDC hydrochloride (1.2 eq) and hydroxybenzotriazole hydrate (1 eq) were added. A suitable base (such as 4-methylmorpholine or triethylamine) (0-1 eq) was added. 15 A catalytic amount (0.1 eq) of 4-dimethylaminopyridine was added. The mixture was stirred at ambient temperature and under a dry atmosphere of nitrogen. After 20 hours, the mixture was concentrated under reduced pressure. The resulting concentrate was partitioned between ethyl acetate and water. The organic portion was separated and washed with aqueous sodium bicarbonate and brine. 20 The organic portion was dried (sodium sulfate) and concentrated under reduced pressure. The crude product was used without purification or was purified by silica gel chromatography and/or crystallization.

25 GENERAL PROCEDURE AL

EDC Coupling

The carboxylic acid was dissolved in methylene chloride. The amino acid (1 eq.), N-methylmorpholine (5 eq.) and hydroxybenzotriazole monohydrate (1.2 eq.) were added in sequence. A cooling bath was applied to the round bottomed flask until the solution reached 0°C. At that time, 1.2 eq. of 1-(3- 30 dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC) was added.

The solution was allowed to stir overnight and come to room temperature under nitrogen pressure. The reaction mixture was worked up by washing the organic phase with saturated aqueous sodium carbonate, 0.1M citric acid, and brine before drying with sodium sulfate. The solvents were then removed to yield crude product. Pure products were obtained by flash chromatography in an appropriate solvent.

GENERAL PROCEDURE AM

Triflate Displacement

To a 0°C solution of *iso*-butyl R-(+)-lactate in CH₂Cl₂ was added 1.1 equivalents of trifluoromethanesulfonic anhydride. After stirring at room temperature for 20 min, 1.1 equivalents of 2,6-lutidine was added and stirring was continued for 10 min. This solution was then transferred to a flask containing 1 equivalent the arylamine and 1 equivalent *N,N*-diisopropylethylamine in CH₂Cl₂ or CH₃NO₂ at 0°C. The reaction was held overnight at room temperature and then stripped free of solvent on a rotary evaporator. The residue was dissolved in ethyl acetate, washed with 5% citric acid, followed by saturated aqueous NaCl, dried over magnesium sulfate or sodium sulfate and then the solution was stripped free of solvent on a rotary evaporator to yield the crude product, which was then purified by chromatography.

GENERAL PROCEDURE AN

BOC Removal

The BOC-protected compound was added to a 1:1 mixture of CH₂Cl₂ and trifluoroacetic acid, and was stirred until tlc indicated complete conversion, typically 2h. The solution was then stripped to dryness and the residue was taken up in ethyl acetate and extracted with dilute HCl. The acid reaction was neutralized and extracted with ethyl acetate. The organic phase was washed with saturated aqueous NaCl and dried over MgSO₄. The solution was stripped free of solvent on a rotary evaporator to yield the product.

GENERAL PROCEDURE AO

Synthesis of Pyruvate Esters

To a mixture of pyruvic acid (8.8 g, 0.1 mol) (Aldrich) in 100 mL of benzene was added *iso*-butanol (14.82 g, 0.2 mol) and a catalytic amount of *p*-toluenesulfonic acid. The mixture was then refluxed using a Dean Stark apparatus. After 4 hours, the reaction appeared to be complete with the isolation of 1.8 g (0.1 mol) of water. The benzene and *iso*-butanol were removed on a rotary evaporator. The residue (14 g, 0.1 mol), which was primarily the pyruvate *iso*-butyl ester by nmr [¹H-Nmr (CDCl₃): δ = 4.0 (d, 2H), 2.5 (s, 3H), 2.0 (m, 1H), 1.0 (d, 6H)], was used without further purification. By substituting other alcohols in place of *iso*-butanol (e.g., ethanol, isopropanol, *n*-butanol, benzyl alcohol and the like), other esters of pyruvic acid can be prepared in a similar manner.

GENERAL PROCEDURE AP

Aromatic Nucleophilic Substitution of Fluorobenzenes

A mixture of 1.82 g (10 mmol) of D,L-alanine *iso*-butyl ester hydrochloride, the fluorobenzene (10 mmol) and 3 g of anhydrous potassium carbonate in 10 mL of DMSO was stirred at 120°C for 2-5 hours. The reaction mixture was then cooled to room temperature and diluted with 100 mL of ethyl acetate. The ethyl acetate extract was washed with water (3x), dried over MgSO₄ and evaporated to dryness to afford the crude product, which was further purified by column chromatography.

GENERAL PROCEDURE AQ

Fourth Transesterification Technique

The ester to be transesterified was dissolved in a large excess of the alcohol and 0.3 equivalents of titanium(IV) isopropoxide (Aldrich) was added. The reaction was followed by tlc until complete and then the volatiles were removed at reduced pressure. The resulting crude material was then chromatographed to obtain the desired product.

GENERAL PROCEDURE AR

Synthesis on *N*-BOC Anilines

To a solution of the aniline in THF was added dropwise 1 equivalent of di-
tert-butyl dicarbonate (Aldrich) in THF and then 1.5 equivalents of 10N aqueous
5 sodium hydroxide at 0°C. After stirring at room temperature for 16 hours, or
heating at 80°C for 3 hours, if needed, the reaction mixture was diluted with
ether and washed with NaHCO₃, brine, dried over sodium sulfate and potassium
carbonate, concentrated at reduced pressure and chromatographed to afford the
N-BOC aniline.

10

GENERAL PROCEDURE AS

Oxime Ester Formation

The trichlorophenyl ester (1 eq.) was stirred in DMF or THF. The oxime
(1.2 eq.) was added and the mixture was stirred at ambient temperature for 1 to
15 4 hours. The resulting mixture was concentrated under reduced pressure and the
residue was purified by silica gel chromatography and/or crystallization.

Example AA

Synthesis of D,L-alanine *iso*-butyl ester hydrochloride

20 A mixture of 35.64 g (0.4 mol) of D,L-alanine (Aldrich), 44 mL (0.6 mol)
of thionyl chloride (Aldrich) and 200 mL of *iso*-butanol was refluxed for 1.5
hours. The volatiles were removed at reduced pressure at 90°C under reduced
pressure to give the title compound as an oil, which was used without further
purification.

25

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 8.72 (br s, 3H), 4.27 (q, J = 7.4 Hz, 1H), 3.95 (m,
2H), 1.96 (s, 1H), 1.73 (d, J = 7.2 Hz, 3H), 0.92 (d, J = 6.7 Hz, 6H).

¹³C-nmr (CDCl₃): δ = 170.0, 72.2, 49.2, 27.5, 18.9, 16.1.

30

Example AB

Synthesis of N-(3,4-dichlorophenyl)alanine

Using the procedure set forth in U.S. Patent No. 3,598,859, the disclosure of which is incorporated herein by reference in its entirety, N-(3,4-dichlorophenyl)alanine was prepared. Specifically, to a solution of 3,4-dichloroaniline (1 equivalent) (Aldrich) in isopropanol (about 500 mL per mole of 3,4-dichloroaniline) is added water (about 0.06 mL per mL of isopropanol) and 2-chloropropionic acid (2 equivalents) (Aldrich). This mixture is warmed to 40°C and sodium bicarbonate (0.25 equivalents) is added in successive portions before heating under reflux for 4-5 days. After cooling, the reaction mixture is poured into water and the unreacted 3,4-dichloroaniline is removed by filtration. The filtrate is acidified to pH 3-4 with concentrated hydrochloric acid and the resultant precipitate is filtered, washed and dried to yield the title compound, m.p. = 148-149°C.

Alternatively, following General Procedure AF above and using N-(3,4-dichlorophenyl)alanine ethyl ester (from Example A1 below), the title compound was prepared.

Example AC

Synthesis of N-(3,5-difluorophenyl)alanine

Using the procedure set forth in U.S. Patent No. 3,598,859, N-(3,5-difluorophenyl)alanine was prepared using 3,5-difluoroaniline (Aldrich) and 2-chloropropionic acid (Aldrich).

Example AD

Synthesis of *Iso*-butyl 2-bromopropionate

To a mixture of *iso*-butanol and 1.0 equivalent of pyridine in dry diethyl ether was added dropwise 1.3 equivalents of 2-bromopropionyl bromide at 0°C. After stirring at room temperature for 16 hours, the reaction was diluted with diethyl ether, washed with 1N HCl, water, aqueous NaHCO₃, brine and dried over magnesium sulfate or sodium sulfate. Removal of the solvents at reduced pressure gave the title compound as a clear oil.

Example AE

Synthesis of N-(2-naphthyl)alanine 2,4,5-trichlorophenyl ester

N-(2-Naphthyl)alanine methyl ester (5.0 g, 20.6 mmol) (from Example A44 below) was dissolved in dioxane (100 mL). NaOH (30 mL, 1N) was added and the resulting solution was stirred for 1 hour. The reaction mixture was concentrated under reduced pressure. The resulting solid was dissolved in water and the aqueous mixture was washed with ether. The aqueous portion was adjusted to pH 3 with 1N HCl and extracted with ethyl acetate. The organic extracts were dried over magnesium sulfate or sodium sulfate and concentrated under reduced pressure to yield a white solid (4.35 g, 98%).

The resulting solid (4.35 g, 20 mmol) was dissolved in dichloromethane (300 mL). 2,4,5-Trichlorophenol (4.9 g, 25 mmol) (Aldrich) was added followed by dicyclohexylcarbodiimide (25 mL, 1M in dichloromethane) (Aldrich). After stirring for 18 hours, the mixture was filtered and concentrated to provide an oil which was purified by chromatography on silica gel using chloroform as the eluant ($R_f = 0.6$). The title compound was obtained as a thick oil which slowly crystallized.

20

Example AI

Synthesis of N-(3,4-dichlorophenyl)alanine ethyl ester

Following General Procedure AA above and using 3,4-dichloroaniline (Aldrich) and ethyl pyruvate (Aldrich), the title compound was prepared as an oil. The reaction was monitored by tlc on silica gel ($R_f = 0.4$ in 25% EtOAc/hexanes) and purification was by preparative plate chromatography (silica gel using 25% EtOAc/hexanes as the eluant).

NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 7.2$ (d, 1H); 6.7 (d, 1H); 6.4 (dd, 1H); 4.30 (bs, 1H); 4.2 (q, 2H); 4.1 (q, 1H); 1.5 (d, 3H); 1.3 (t, 3H).

^{13}C -nmr (CDCl_3): $\delta = 175$; 146.7; 133; 131; 121; 114.9; 112.6; 72.0; 52.4; 28.3; 19.5.

$C_{11}H_{13}Cl_2NO_2$ (MW = 262.14).

Example A2

Synthesis of N-(3-trifluoromethyl-4-chlorophenyl)alanine ethyl ester

5 Following General Procedure AA above and using 4-chloro-3-(trifluoromethyl)aniline (Aldrich) and ethyl pyruvate (Aldrich), the title compound was prepared.

Analysis: Calc.: C, 48.74; H, 4.43; N, 4.74. Found: C, 48.48; H, 4.54; N, 4.94.

10 $C_{12}H_{13}F_3ClNO_2$ (MW = 295.69); mass spectroscopy (MH^+) 295.

Example A3

Synthesis of N-(3,5-dichlorophenyl)alanine ethyl ester

15 Following General Procedure AA above and using 3,5-dichloroaniline (Aldrich) and ethyl pyruvate (Aldrich), the title compound was prepared.

Analysis: Calc.: C, 50.40; H, 5.00; N, 5.34. Found: C, 50.50; H, 5.06; N, 5.25.

$C_{11}H_{13}Cl_2NO_2$ (MW = 262.14); mass spectroscopy (MH^+) NA.

20

Example A4

Synthesis of N-(3,4-difluorophenyl)alanine ethyl ester

25 Following General Procedure AA above and using 3,4-difluoroaniline (Aldrich) and ethyl pyruvate (Aldrich), the title compound was prepared. The reaction was monitored by tlc on silica gel (R_f = 0.4 in 25% EtOAc/hexanes) and purification was by preparative plate chromatography (silica gel using 25% EtOAc/hexanes as the eluant).

NMR data was as follows:

1H -nmr ($CDCl_3$): δ = 7.4 (m, 1H), 6.8 (d, 1H), 6.5 (m, 1H), 4.30 (bs, 1H), 4.2 (q, 2H), 4.1 (q, 1H), 1.5 (d, 3H), 1.3 (t, 3H).

30 ^{13}C -nmr ($CDCl_3$): δ = 175, 146.7, 135, 132, 125, 116, 113, 72, 52, 28, 19.

$C_{11}H_{13}F_2NO_2$ (MW = 229.23); mass spectroscopy (MH^+) 230.

Example A5

Synthesis of N-(3,4-dichlorophenyl)alanine benzyl ester

Following General Procedure AA above and using 3,4-dichloroaniline (Aldrich) and benzyl pyruvate (prepared by following General Procedure AO above using benzyl alcohol in place of *iso*-butanol), the title compound was prepared as an oil. The reaction was monitored by tlc on silica gel ($R_f = 0.4$ in 25% EtOAc/hexanes) and purification was by preparative plate chromatography (silica gel using 25% EtOAc/hexanes as the eluant).

NMR data was as follows:

¹H-nmr (CDCl₃): $\delta = 7.18$ (d, 1H); 7.0 (m, 5H); 6.6 (d, 1H); 6.4 (dd, 1H); 5.1 (s, 2H); 4.30 (bs, 1H); 4.08 (q, 1H); 1.94 (m, 1H); 1.47 (d, 3H); 0.91 (d, 6H).

¹³C-nmr (CDCl₃): $\delta = 174.5$; 146.7; 133.5; 131.3; 121.3; 120.1; 114.9; 113.6; 72.0; 60.1; 52.4; 28.3; 19.5; 19.3.

C₁₆H₁₅Cl₂NO₂ (MW = 324.31); mass spectroscopy (MH⁺) 325.

Example A6

Synthesis of N-(3,4-dichlorophenyl)alanine *iso*-butyl ester

Following General Procedure AA above and using 3,4-dichloroaniline (Aldrich) and *iso*-butyl pyruvate (prepared by following General Procedure AO above), the title compound was prepared as an oil. The reaction was monitored by tlc on silica gel ($R_f = 0.55$ in 25% EtOAc/hexanes) and purification was by preparative plate chromatography (silica gel using 25% EtOAc/hexanes as the eluant).

NMR data was as follows:

¹H-nmr (CDCl₃): $\delta = 7.18$ (d, 1H, $J=8.7$ Hz), 6.66 (d, 1H, $J=2.7$ Hz), 6.43 (dd, 1H, $J = 8.7$ Hz, $J = 2.7$ Hz), 4.30 (bs, 1H), 4.08 (q, 1H, $J = 6.9$ Hz), 1.94 (sept, 1H, $J = 6.7$ Hz), 1.47 (d, 3H, $J = 6.9$ Hz), 0.91 (d, 6H, $J = 6.6$ Hz).

¹³C-nmr (CDCl₃) $\delta = 174.5$, 146.7, 133.5, 131.3, 121.3, 114.9, 113.6, 72.0, 52.4, 28.3, 19.5, 19.3.

$C_{13}H_{17}Cl_2NO_2$ (MW = 290.19); mass spectroscopy (MH^+) 290.

Example A7

Synthesis of N-(3,4-dichlorophenyl)alanine *iso*-propyl ester

5 Following General Procedure AA above and using 3,4-dichloroaniline (Aldrich) and isopropyl pyruvate (prepared by following General Procedure AO above using isopropanol in place of *iso*-butanol), the title compound was prepared as an oil. The reaction was monitored by tlc on silica gel (R_f = 0.4 in 25% EtOAc/hexanes) and purification was by preparative plate chromatography
10 (silica gel using 25% EtOAc/hexanes as the eluant).

NMR data was as follows:

1H -nmr ($CDCl_3$): δ = 7.18 (d, 1H); 6.66 (d, 1H); 6.43 (dd, 1H); 4.30 (bs, 1H); 4.08 (m, 1H); 1.94 (m, 1H); 1.47 (d, 3H); 0.91 (d, 6H).

^{13}C -nmr ($CDCl_3$): δ = 174.5; 146.7; 133.5; 131.3; 121.3; 114.9; 113.6; 72.0;
15 52.4; 19.5.

$C_{12}H_{15}Cl_2NO_2$ (MW = 276.16); mass spectroscopy (MH^+) 277.

Example A8

Synthesis of N-(3,4-dichlorophenyl)alanine *n*-butyl ester

20 Following General Procedure AA above and using 3,4-dichloroaniline (Aldrich) and *n*-butyl pyruvate (prepared by following General Procedure AO above using *n*-butanol in place of *iso*-butanol), the title compound was prepared. The reaction was monitored by tlc on silica gel (R_f = 0.7 in 25% EtOAc/hexanes) and purification was by preparative plate chromatography (silica
25 gel using 25% EtOAc/hexanes as the eluant).

NMR data was as follows:

1H -nmr ($CDCl_3$): δ = 7.18 (d, 1H); 6.66 (d, 1H); 6.43 (dd, 1H); 4.30 (bs, 1H); 4.2 (m, 2H); 4.08 (q, 1H); 1.94 (m, 1H); 1.47 (m, 4H); 0.91 (t, 3H).

^{13}C -nmr ($CDCl_3$): δ = 174.5; 146.7; 133.5; 131.3; 121.3; 114.9; 113.6; 72.0;
30 52.4; 28.3; 20.2; 19.5.

$C_{13}H_{17}Cl_2NO_2$ (MW = 290.19); mass spectroscopy (MH^+) 291.

Example A9

Synthesis of N-(3,4-dichlorophenyl)alanine methyl ester (R,S isomers)

5

Following General Procedure AA above and using 3,4-dichloroaniline (Aldrich) and methyl pyruvate (Aldrich), the title compound was prepared as an oil. The reaction was monitored by tlc on silica gel ($R_f = 0.55$ in 25% EtOAc/hexanes) and purification was by flash chromatography (silica gel using

10

NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 7.19$ (d, $J = 8.73$ Hz, 1H), 6.66 (d, $J = 2.75$ Hz, 1H), 6.43 (dd, $J = 8.73$ Hz, 2.80 Hz, 1H), 4.25 (bd, $J = 8.25$ Hz, 1H), 4.08 (m, 1H), 3.76 (s, 3H), 1.47 (d, $J = 6.90$ Hz).

15

^{13}C -nmr (CDCl_3) $\delta = 174.35, 145.96, 132.87, 130.70, 120.76, 114.38, 112.90, 52.43, 51.70, 18.67$.

$\text{C}_{10}\text{H}_{11}\text{Cl}_2\text{NO}_2$ (MW = 248.11); mass spectroscopy (MH^+) 247.

Example A10

20

Synthesis of N-(3,4-dichlorophenyl)alanine cyclopentyl ester

Following transesterification General Procedure AB above and using N-(3,4-dichlorophenyl)alanine methyl ester (from Example A9 above) and cyclopentanol (Aldrich), the title compound was prepared as an oil. The reaction was monitored by silica gel tlc ($R_f = 0.66$ in 25% EtOAc/hexanes). Purification was by preparative plate chromatography (silica gel using 25% EtOAc/hexanes as the eluant).

25

NMR data was as follows:

30

^1H -nmr (CDCl_3): $\delta = 7.19$ (d, 1H, $J = 8.7$ Hz), 6.66 (d, 1H, $J = 2.7$ Hz), 6.43 (dd, 1H, $J = 8.7$ Hz, $J = 2.7$ Hz), 5.22 (m, 1H), 4.27 (d, 1H, $J = 8.1$ Hz), 4.02 (quint, 1H, $J = 7.5$ Hz), 1.74 (m, 8H), 1.43 (d, 3H, $J = 6.9$ Hz).

^{13}C -nmr (CDCl_3): $\delta = 174.3, 146.7, 133.4, 131.2, 121.2, 114.9, 113.7, 78.9, 52.5, 33.2, 24.2, 24.1, 19.1$.

$\text{C}_{14}\text{H}_{17}\text{Cl}_2\text{NO}_2$ (MW = 302.20); mass spectroscopy (MH^+) 301.

5

Example A11

Synthesis of N-(3,4-dichlorophenyl)alanine *n*-propyl ester

Following General Procedure AA above and using 3,4-dichloroaniline (Aldrich) and *n*-propyl pyruvate (prepared by following General Procedure AO above using *n*-propanol in place of *iso*-butanol), the title compound was prepared as an oil. The reaction was monitored by tlc on silica gel ($R_f = 0.5$ in 25% EtOAc/hexanes) and purification was by preparative plate chromatography (silica gel using 25% EtOAc/hexanes as the eluant).

NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 7.2$ (d, 1H); 6.6 (d, 1H); 6.4 (dd, 1H); 4.30 (bs, 1H); 4.2 (q, 2H); 4.08 (q, 1H); 1.94 (m, 2H); 1.5 (d, 3H); 0.95 (t, 3H).

^{13}C -nmr (CDCl_3): $\delta = 178; 144.7; 130.2; 120.62; 115.11; 71.82; 52.90$.

$\text{C}_{12}\text{H}_{15}\text{Cl}_2\text{NO}_2$ (MW = 276.16); mass spectroscopy (MH^+) 277.

20

Example A12

Synthesis of N-(3,4-dichlorophenyl)alanine allyl ester

Following transesterification General Procedure AB above and using N-(3,4-dichlorophenyl)alanine methyl ester (from Example A9 above) and allyl alcohol (Aldrich), the title compound was prepared as an oil. The reaction was monitored by silica gel tlc ($R_f = 0.62$ in 25% EtOAc/hexanes). Purification was by preparative plate chromatography (silica gel using 25% EtOAc/hexanes as the eluant).

30

NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 7.19$ (d, 1H, $J = 8.7$ Hz), 6.67 (d, 1H, $J = 2.8$ Hz), 6.44 (dd, 1H, $J = 8.7$ Hz, $J = 2.8$ Hz), 5.90 (m, 1H), 5.30 (m, 2H), 4.64 (m, 2H), 4.26 (m, 1H), 4.10 (m, 1H), 1.48 (d, 3H, $J = 6.9$ Hz).

¹³C-nmr (CDCl₃): δ = 174.1, 146.6, 133.5, 132.1, 131.3, 121.4, 119.6, 115.0, 113.6, 66.5, 52.4, 19.3.

C₁₂H₁₃Cl₂NO₂ (MW = 274.15); mass spectroscopy (MH⁺) 273.

5

Example A13

Synthesis of N-(3,4-dichlorophenyl)alanine 4-methylpentyl ester

Following transesterification General Procedure AB above and using N-(3,4-dichlorophenyl)alanine methyl ester (from Example A9 above) and 4-methylpentanol (Aldrich), the title compound was prepared as an oil. The reaction was monitored by silica gel tlc (R_f = 0.70 in 25% EtOAc/hexanes). Purification was by preparative plate chromatography (silica gel using 25% EtOAc/hexanes as the eluant).

15

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.18 (d, 1H, J = 8.7 Hz), 6.66 (d, 1H, J = 2.7 Hz), 6.43 (dd, 1H, J = 8.7 Hz, J = 2.7 Hz), 4.28 (m, 1H), 4.10 (m, 3H), 1.55 (m, 6H), 1.19 (m, 2H), 0.87 (d, 3H, J = 6.6 Hz).

¹³C-nmr (CDCl₃): δ = 174.6, 146.7, 133.4, 131.3, 121.3, 115.0, 113.6, 66.4, 52.4, 35.4, 28.2, 27.0, 23.0, 19.3.

20

C₁₅H₂₁Cl₂NO₂ (MW = 318.25); mass spectroscopy (MH⁺) 317.

Example A14

Synthesis of N-(3,4-dichlorophenyl)alanine 2,2-dimethyl-1,3-dioxolane-4-methyl ester

25

Following transesterification General Procedure AB above and using N-(3,4-dichlorophenyl)alanine methyl ester (from Example A9 above) and 2,2-dimethyl-1,3-dioxolane-4-methanol (solketal) (Aldrich), the title compound was prepared as a mixture of diastereomers. The reaction was monitored by silica gel tlc (R_f = 0.32 in 25% EtOAc/hexanes). Purification was by preparative plate chromatography (silica gel using 25% EtOAc/hexanes as the eluant).

30

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.19 (d, 1H, J = 8.7 Hz), 6.66 (d, 1H, 2.7 Hz), 6.43 (dd, 1H, J = 8.7 Hz, J = 2.7 Hz), 4.22 (m, 6H), 3.70 (m, 1H), 1.43 (m, 9H).

¹³C-nmr (CDCl₃): δ = 174.34, 174.32, 146.5, 133.5, 131.3, 121.5, 115.0, 113.6, 110.52, 110.51, 73.97, 73.89, 66.6, 66.01, 65.95, 52.42, 52.37, 27.3, 25.8, 19.3.

C₁₅H₁₉Cl₂NO₄ (MW = 348.23); mass spectroscopy (MH⁺) 347.

Example A15

Synthesis of N-(3,4-dichlorophenyl)alanine cyclohexylmethyl ester

Following transesterification General Procedure AB above and using N-(3,4-dichlorophenyl)alanine methyl ester (from Example A9 above) and cyclohexylmethanol (Aldrich), the title compound was prepared.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.19 (d, 1H), 6.68 (d, 1H), 6.45 (dd, 1H), 4.26 (bd, 1H), 4.10 (m, 1H), 3.95 (d, 2H), 1.70-1.55 (m, 6H), 1.50 (d, 3H), 1.35-0.85 (m, 5H).

¹³C-nmr (CDCl₃): δ = 174.58, 146.72, 133.48, 131.27, 121.34, 114.98, 113.72, 71.06, 52.52, 37.68, 30.10, 26.83, 26.17, 19.32.

C₁₅H₂₁Cl₂NO₂ (MW = 318.25); mass spectroscopy (MH⁺) 317.

Example A16

Synthesis of N-(3,4-dichlorophenyl)alanine *tert*-butyloxycarbonylmethyl ester

Following General Procedure AE above and using N-(3,4-dichlorophenyl)alanine (from Example AB above) and *tert*-butyl bromoacetate (Aldrich), the title compound was prepared as a solid. The reaction was monitored by silica gel tlc (R_f = 0.57 in 25% EtOAc/hexanes). Purification was by recrystallization from ethanol.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.19 (d, 1H), 6.68 (d, 1H), 6.45 (dd, 1H), 4.55 (m, 2H), 4.20 (m, 2H), 1.55 (d, 3H), 1.45 (s, 9H).

^{13}C -nmr (CDCl_3): $\delta = 173.9, 166.9, 146.5, 133.5, 131.3, 115.1, 113.6, 83.4, 62.2, 52.2, 28.6, 19.3$.

$\text{C}_{15}\text{H}_{19}\text{Cl}_2\text{NO}_4$ (MW = 348.23); mass spectroscopy (MH^+) 347.

5

Example A17

Synthesis of N-(3,4-dichlorophenyl)leucine *iso*-butyl ester

Following General Procedure AA above and using 3,4-dichloroaniline (Aldrich) and *iso*-butyl 4-methyl-2-oxopentanoate (prepared by following General Procedure AO above using 4-methyl-2-oxovaleric acid (Fluka) and *iso*-butanol), the title compound was prepared as an oil. The reaction was monitored by tlc on silica gel ($R_f = 0.6$ in 25% EtOAc/hexanes) and purification was by preparative plate chromatography (silica gel using 25% EtOAc/hexanes as the eluant).

NMR data was as follows:

15 ^1H -nmr (CDCl_3): $\delta = 7.2$ (d, 1H); 6.5 (d, 1H); 6.4 (dd, 1H); 4.30 (bs, 1H); 4.08 (q, 1H); 3.8(m, 2H); 1.8 (m, 3H); 0.91 (m, 12H).

^{13}C -nmr (CDCl_3): $\delta = 174.5; 146.7; 133.5; 131.3; 121.3; 114.9; 113.6; 72.0; 52; 28.3; 20.1; 19.5$.

$\text{C}_{16}\text{H}_{23}\text{Cl}_2\text{NO}_2$ (MW = 332.27); mass spectroscopy (MH^+) 333.

20

Example A18

Synthesis of 2-[N-(3,4-dichlorophenyl)amino]pentanoic acid *iso*-butyl ester

Following General Procedure AA above and using 3,4-dichloroaniline (Aldrich) and *iso*-butyl 2-oxopentanoate (prepared by following General Procedure AO above using 2-oxovaleric acid (Fluka) and *iso*-butanol), the title compound was prepared as an oil. The reaction was monitored by tlc on silica gel ($R_f = 0.5$ in 25% EtOAc/hexanes) and purification was by preparative plate chromatography (silica gel using 25% EtOAc/hexanes as the eluant).

NMR data was as follows:

30 ^1H -nmr (CDCl_3): $\delta = 7.2$ (d, 1H); 6.6 (d, 1H); 6.4 (dd, 1H); 4.3 (d, 1H); 3.8 (m, 3H); 1.9 (m, 6H); 1.0 (t, 3H), 0.9 (m, 6H).

^{13}C -nmr (CDCl_3): $\delta = 178; 144.7; 130.2; 120.62; 115.11; 71.82; 52.90; 28.30; 19.53$.

$\text{C}_{15}\text{H}_{21}\text{Cl}_2\text{NO}_2$ (MW = 318.3); mass spectroscopy (MH^+) 319.

5

Example A19

Synthesis of N-(4-cyanophenyl)alanine *iso*-butyl ester

Following General Procedure AP above and using 4-fluorobenzonitrile (Aldrich) and D,L-alanine *iso*-butyl ester hydrochloride (from Example AA above), the title compound was prepared as an oil. The product was recovered by column chromatography on silica gel using 1:5 EtOAc/hexanes as the eluant.

NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 7.44$ (d, $J = 8.8$ Hz, 2H), 6.57 (d, $J = 8.8$ Hz, 2H), 4.74 (d, $J = 8.1$ Hz, 1H), 4.18 (t, $J = 7.4$ Hz, 1H), 3.95 (m, 2H), 1.94 (m, 1H), 1.51 (d, $J = 6.9$ Hz, 3H), 0.91 (d, $J = 6.7$ Hz, 6H).

15

^{13}C -nmr (CDCl_3): $\delta = 173.4, 149.7, 133.8, 120.1, 112.7, 99.8, 71.6, 51.2, 27.7, 18.9, 18.6$.

$\text{C}_{14}\text{H}_{18}\text{N}_2\text{O}_2$ MW = 246.31; mass spectroscopy (MH^+) 247.

Example A20

20

Synthesis of N-(3-chloro-4-cyanophenyl)alanine *iso*-butyl ester

Following General Procedure AP above and using 2-chloro-4-fluorobenzonitrile (Aldrich) and D,L-alanine *iso*-butyl ester hydrochloride (from Example AA above), the title compound was prepared. The product was recovered by column chromatography on silica gel using 1:5 EtOAc/hexanes as the eluant.

25

NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 7.40$ (d, $J = 8.5$ Hz, 1H), 6.62 (d, $J = 2.3$ Hz, 1H), 6.48 (dd, $J = 2.4, 8.6$ Hz, 1H), 4.90 (d, $J = 7.6$ Hz, 1H), 4.16 (quintet, $J = 7.1$ Hz, 1H), 3.96 (dd, $J = 2.2, 6.7$ Hz, 2H), 1.97 (m, 1H), 1.51 (d, $J = 7.0$ Hz, 3H), 0.93 (d, $J = 6.7$ Hz, 6H).

30

^{13}C -nmr (CDCl_3): $\delta = 173.0, 150.4, 138.3, 134.9, 117.3, 112.8, 111.3, 100.6, 71.7, 51.1, 27.7, 18.9, 18.4$.

$\text{C}_{14}\text{H}_{17}\text{N}_2\text{O}_2\text{Cl}$ MW = 280.76; mass spectroscopy (MH^+) 281.

5

Example A21

Synthesis of N-(3,4-dichloro)alanine *iso*-butyl ester (S isomer)

Following General Procedure AM above and using 3,4-dichloroaniline
10 (Aldrich) and *iso*-butyl R-(+)-lactate (Aldrich), the title compound was prepared as an oil. The reaction was monitored by silica gel tlc ($R_f = 0.55$ in 25% EtOAc/hexanes). Purification was column chromatography.

NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 7.19$ (d, $J = 8.73$, 1H), 6.67 (d, $J = 2.75$, 1H), 6.45
15 (dd, $J = 8.73$, $J = 2.75$, 1H), 4.28 (bd, $J = 8.36$, 1H), 4.09 (quint, 1H), 3.94 (d, $J = 6.66$, 2H), 1.95 (hept, $J = 6.71$, 1H), 1.49 (d, $J = 6.90$, 3H), 0.92 (d, $J = 6.04$, 6H).

^{13}C -nmr (CDCl_3): $\delta = 174.57, 146.67, 133.47, 131.28, 121.29, 114.93, 113.63, 71.01, 52.43, 28.30, 19.55, 19.33$.

20 $\text{C}_{13}\text{H}_{17}\text{Cl}_2\text{NO}_2$ (MW = 290.19); mass spectroscopy (MH^+) 290.

Example A22

Synthesis of N-(3,4-dichloro)alanine tetrahydrofuran-3-yl-methyl ester

25

Following transesterification General Procedure AB above and using N-(3,4-dichlorophenyl)alanine methyl ester (from Example A9 above) and tetrahydro-3-furanmethanol (Aldrich), the title compound was prepared as an oil. The reaction was monitored by silica gel tlc ($R_f = 0.33$ in 25% EtOAc/hexanes).
30 Purification was by preparative plate chromatography (silica gel using 25% EtOAc/hexanes as the eluant).

NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 7.18$ (d, 1H, $J = 8.7$ Hz), 6.65 (d, 1H, $J = 2.7$ Hz), 6.42 (dd, 1H, $J = 8.7$ Hz, $J = 2.7$ Hz), 4.30 (m, 1H), 4.09 (m, 3H), 3.78 (m,

3H), 3.53 (m, 1H), 2.56 (m, 1H), 1.94 (m, 1H), 1.58 (m, 1H), 1.46 (d, 3H, J = 6.9 Hz).

¹³C-nmr (CDCl₃): δ = 174.5, 146.6, 133.5, 131.3, 121.4, 114.9, 113.6, 70.86, 70.83, 68.2, 67.31, 67.29, 52.4, 38.7, 29.36, 29.33, 19.2.

5 C₁₄H₁₇Cl₂NO₃ (MW = 318.20); mass spectroscopy (MH⁺) 318.

Example A23

Synthesis of N-(3,5-dichlorophenyl)alanine *n*-propyl ester

Following General Procedure AA above and using 3,5-dichloroaniline
10 (Aldrich) and *n*-propyl pyruvate (which can be prepared by following General Procedure AO above using *n*-propanol in place of *iso*-butanol), the title compound could be prepared.

Example A24

15 Synthesis of 2-[N-(3,4-dichlorophenyl)amino]butanoic acid *iso*-butyl ester

Following General Procedure AA above and using 3,4-dichloroaniline
(Aldrich) and *iso*-butyl 2-oxobutanoate (prepared by following General
Procedure AO above using 2-oxobutyric acid (Aldrich) and *iso*-butanol), the title
compound was prepared as an oil. The reaction was monitored by tlc on silica
20 gel (R_f = 0.3 in 25% EtOAc/hexanes) and purification was by preparative plate chromatography (silica gel using 25% EtOAc/hexanes as the eluant).

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.2 (d, 1H); 6.6 (d, 1H); 6.4 (dd, 1H); 4.3 (d, 1H);
3.8 (m, 3H); 1.9 (m, 3H); 1.0 (t, 3H); 0.9(m, 6H).

25 ¹³C-nmr (CDCl₃): δ = 178; 144.7; 130.2; 120.62; 115.11; 71.82; 52.90;
28.30; 20.5; 19.53.

C₁₄H₁₉Cl₂NO₂ (MW = 304.22); mass spectroscopy (MH⁺) 305.

Example A25

Synthesis of N-(4-chlorophenyl)alanine *iso*-butyl ester

Following General Procedure AA above and using 4-chloroaniline (Aldrich) and *iso*-butyl pyruvate (prepared by following General Procedure AO above), the title compound was prepared as an oil. The reaction was monitored by tlc on silica gel ($R_f = 0.6$ in 25% EtOAc/hexanes) and purification was by preparative plate chromatography (silica gel using 25% EtOAc/hexanes as the eluant).

NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 7.18$ (d, 2H), 6.66 (d, 2H), 4.30 (bs, 1H), 4.08 (q, 1H), 1.94 (sept, 1H), 1.47 (d, 3H), 0.91 (d, 6H).

^{13}C -nmr (CDCl_3): $\delta = 174.5, 146.7, 133.5, 131.3, 121.3, 114.9, 113.6, 72.0, 52.4, 28.3, 19.5, 19.3$.

$\text{C}_{13}\text{H}_{18}\text{ClNO}_2$ (MW = 255.75); mass spectroscopy (MH^+) 256.

Example A26

Synthesis of N-(3,5-dichlorophenyl)alanine *iso*-butyl ester

Following General Procedure AA above and using 3,5-dichloroaniline (Aldrich) and *iso*-butyl pyruvate (prepared by following General Procedure AO above), the title compound was prepared as an oil. The reaction was monitored by tlc on silica gel ($R_f = 0.4$ in 25% EtOAc/hexanes) and purification was by preparative plate chromatography (silica gel using 25% EtOAc/hexanes as the eluant).

NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 7.18$ (d, 2H), 6.66 (m, 1H), 4.30 (bs, 1H), 4.08 (q, 1H), 1.94 (m, 1H), 1.47 (d, 3H), 0.91 (d, 6H).

^{13}C -nmr (CDCl_3): $\delta = 175; 146.7; 133; 131; 121; 114.9; 112.6; 72.0; 52.4; 28.3; 19.5$.

$\text{C}_{13}\text{H}_{17}\text{Cl}_2\text{NO}_2$ (MW = 290.2); mass spectroscopy (MH^+) 291.

Example A27

Synthesis of N-(4-ethylphenyl)alanine methyl ester

A solution of 0.68 g (5 mmol) of 4'-aminoacetophenone (Aldrich), 0.60 mL of 90% methyl pyruvate (Aldrich) and 0.05 g (0.25 mmol) of *p*-toluenesulfonic acid in ethanol was hydrogenated in the presence of a catalytic amount of 10% Pd/C at from 30 to 15 psi of hydrogen for 16 hours. The catalyst was removed by filtering the reaction mixture through Celite and the solvent was evaporated to provide the crude product. The product was purified by column chromatography (silica gel using 1:9 EtOAc/hexanes as the eluant) to provide the title compound.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 1.19 (t, J = 7.6 Hz, 3H), 1.47 (d, J = 6.8 Hz, 3H), 2.54 (q, J = 7.6 Hz, 2H), 3.74 (s, 3H), 4.04 (bs, 1H), 4.13 (m, 1H), 6.57 (d, J = 8.5 Hz, 2H), 7.03 (d, J = 8.4 Hz, 2H).

¹³C-nmr (CDCl₃): δ = 15.8, 18.0, 27.9, 52.17, 52.19, 113.5, 128.6, 134.1, 144.4, 175.3.

C₁₂H₁₇NO₂ MW = 207.27; mass spectroscopy (MH⁺) 208.

Example A28

Synthesis of N-(4-(1-ethoxy)ethylphenyl)alanine methyl ester

Following the procedure for Example A27 above, the title compound was isolated as another reaction product by column chromatography (silica gel using 1:9 EtOAc/hexanes as the eluant).

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 1.15 (t, J = 7.0 Hz, 3H), 1.40 (d, J = 6.5 Hz, 3H), 1.47 (d, J = 6.1 Hz, 3H), 3.31 (q, J = 5.1 Hz, 2H), 3.74 (s, 3H), 4.14 (m, 2H), 4.29 (q, J = 6.4 Hz, 1H), 6.57 (d, J = 8.5 Hz, 2H), 7.12 (d, J = 8.4 Hz, 2H).

¹³C-nmr (CDCl₃): δ = 15.4, 19.0, 23.9, 51.9, 52.2, 63.4, 77.3, 113.1, 127.3, 133.6, 145.8, 175.1.

C₁₄H₂₁NO₃ MW = 251.33; mass spectroscopy (MH⁺) 251.

Example A29

**Synthesis of N-(3,4-dichloro)alanine 2,2-dimethylpropyl ester
(R,S isomers)**

5 Following transesterification General Procedure AQ above and using N-(3,4-dichlorophenyl)alanine methyl ester (from Example A9 above) and neopentyl alcohol (Aldrich), the title compound was prepared. The reaction was monitored by silica gel tlc ($R_f = 0.72$ in 25% EtOAc/hexanes). Purification was by flash chromatography (silica gel using 25% EtOAc/hexanes as the eluant).

10 NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 7.19$ (d, 1H, $J = 8.7$ Hz), $\delta = 6.68$ (d, 1H, $J = 2.7$ Hz), 6.45 (dd, 1H, $J = 8.7$ Hz, $J = 2.7$ Hz), 4.29 (m, 1H), 4.11 (m, 1H), 3.85 (m, 2H), 1.49 (d, 3H, $J = 6.9$ Hz), 0.93 (s, 9H).

^{13}C -nmr (CDCl_3): $\delta = 174.6, 146.7, 133.5, 131.3, 121.3, 114.9, 113.7, 75.2,$
15 52.4, 32.0, 26.9, 19.4.

$\text{C}_{14}\text{H}_{19}\text{Cl}_2\text{NO}_2$ (MW = 304.22); mass spectroscopy (MH^+) 303.

Example A30

Synthesis of N-(3,4-dichlorophenyl)glycine *iso*-butyl ester

20 3,4-Dichloroaniline (Aldrich) was treated with di-*tert*-butyl dicarbonate (Aldrich) using conventional procedures to produce the N-BOC aniline. The N-BOC aniline was treated with sodium hydride in THF and then with *iso*-butyl 2-bromoacetate (from Example AD above) to produce the N-BOC N-(3,4-dichlorophenyl)glycine *iso*-butyl ester. The BOC group was then removed using
25 General Procedure AN above to afford the title compound. The reaction was monitored by tlc on silica gel ($R_f = 0.78$ in 50% EtOAc/hexanes) and purification was by preparative plate chromatography (silica gel using 50% EtOAc/hexanes as the eluant).

NMR data was as follows:

30 ^1H -nmr (CDCl_3): $\delta = 7.19$ (dd, $J=4.1, 4.7, 3.4$, 1H); 6.65 (d, $J=2.7$, 1H); 6.44 (dd, $J=2.7, 4.5, 4.2$, 1H); 4.4 (m, 1H); 3.97 (dd, $J=3.6, 3.0, 2.3$, 2H); 3.87 (s, 2H); 1.9 (m, 1H); 0.93 (d, $J=6.7$, 6H).

^{13}C -nmr (CDCl_3): δ = 171.2, 147.0, 133.5, 131.3, 121.2, 114.5, 113.3, 72.2, 46.0, 28.2, 19.6.

$\text{C}_{12}\text{H}_{15}\text{Cl}_2\text{NO}_2$ (MW = 276); mass spectroscopy (MH^+) 277.

5

Example A31

Synthesis of N-(3,4-dichlorophenyl)alanine 2-ethylbutyl ester

Following General Procedure AA above and using 3,4-dichloroaniline (Aldrich) and 2-ethylbutyl pyruvate (prepared by following General Procedure AO above using 2-ethylbutanol (Aldrich) in place of *iso*-butanol), the title
10 compound was prepared as an oil. The reaction was monitored by tlc on silica gel (R_f = 0.6 in 25% EtOAc/hexanes) and purification was by preparative plate chromatography (silica gel using 25% EtOAc/hexanes as the eluant).

NMR data was as follows:

^1H -nmr (CDCl_3): δ = 7.2 (d, 1H); 6.6 (d, 1H); 6.4 (dd, 1H); 4.2 (t, 2H); 4.1
15 (q, 1H); 1.5 (d, 3H); 1.4 (m, 4H); 1.0 (m, 6H).

^{13}C -nmr (CDCl_3): δ = 178; 144.7; 130.2; 120.62; 115.11; 70.7; 51.90; 26.3; 19.53, 18.5.

$\text{C}_{15}\text{H}_{21}\text{Cl}_2\text{NO}_2$ (MW = 318.25); mass spectroscopy (MH^+) 319.

20

Example A32

Synthesis of N-(3-chloro-4-iodophenyl)alanine *iso*-butyl ester

Following General Procedure AR above and using 3-chloro-4-iodoaniline (Aldrich), *N*-BOC-3-chloro-4-iodoaniline was prepared. To a stirred slurry of 5.0 equivalents of sodium hydride in DMF was added 1.0 equivalent of *N*-BOC-
25 3-chloro-4-iodoaniline and then 1.1 equivalents of *iso*-butyl 2-bromopropionate (from Example AD above) were slowly added. The reaction was heated to 100°C for 10 hours, cooled, diluted with dichloromethane and washed with cold 1N HCl, water and brine. The solvents were removed at reduced pressure and the residue was chromatographed to provide *N*-BOC-*N*-(3-chloro-4-
30 iodophenyl)alanine *iso*-butyl ester as a clear oil. Following General Procedure AN above, the BOC group was removed from *N*-BOC-*N*-(3-chloro-4-

iodophenyl)alanine *iso*-butyl ester to provide the title compound. The BOC-removal reaction was monitored by tlc on silica gel ($R_f = 0.58$ in 30% EtOAc/hexanes) and purification was by preparative plate chromatography (silica gel using 30% EtOAc/hexanes as the eluant). The compound was further
5 purified by chromatography on an HPLC chiral column (Chiralcel OD).

NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 7.52$ (d, $J=8.7$, 1H); 6.72 (d, $J=2.7$, 1H); 6.25 (dd, $J=2.7$, 5.9, 2.7, 1H); 4.35 (d, $J=6.6$, 1H); 4.08 (quintex, $J=7.2$, 6.7, 1H); 3.93 (d, $J=6.7$, 2H); 1.94 (m, 1H); 1.47 (d, $J=6.9$, 3H); 0.92 (d, $J=6.9$, 6H).

10 ^{13}C -nmr (CDCl_3): $\delta = 174.5$, 148.3, 140.7, 139.5, 114.4, 114.3, 82.6, 72.0, 52.2, 28.3, 19.6, 19.3.

$\text{C}_{13}\text{H}_{17}\text{ClINO}_2$ (MW = 381.5); mass spectroscopy (MH^+) 382.

Example A33

15 **Synthesis of N-(4-azidophenyl)alanine *iso*-butyl ester**

Following General Procedure AA above and using 4-azidoaniline (Aldrich) and *iso*-butyl pyruvate (prepared by following General Procedure AO above), the title compound was prepared as an oil. The reaction was monitored by tlc on silica gel ($R_f = 0.3$ in 25% EtOAc/hexanes) and purification was by
20 preparative plate chromatography (silica gel using 25% EtOAc/hexanes as the eluant).

NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 7.3$ (d, 2H), 6.8 (d, 2H), 4.30 (bs, 1H), 4.08 (q, 1H), 1.94 (sept, 1H), 1.47 (d, 3H), 0.91 (d, 6H).

25 ^{13}C -nmr (CDCl_3): $\delta = 174.5$, 148.7, 131.5, 130.3, 121.3, 114.9, 113.6, 72.0, 52.4, 28.3, 19.5, 19.3.

$\text{C}_{13}\text{H}_{18}\text{N}_4\text{O}_2$ (MW = 262.31); mass spectroscopy (MH^+) 263.

Example A34

30

Synthesis of

N-[(4-phenylcarbonyl)phenyl]alanine *iso*-butyl ester

Following General Procedure AA above and using 4'-aminobenzophenone (Aldrich) and *iso*-butyl pyruvate (prepared by following General Procedure AO above), the title compound was prepared as an oil. The reaction was monitored by tlc on silica gel ($R_f = 0.4$ in 25% EtOAc/hexanes) and purification was by preparative plate chromatography (silica gel using 25% EtOAc/hexanes as the eluant).

NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 7.7$ (d, 2H), 7.1 (m, 5H), 6.9 (d, 2H), 4.30 (bs, 1H), 4.08 (q, 1H), 1.94 (sept, 1H), 1.47 (d, 3H), 0.91 (d, 6H).

^{13}C -nmr (CDCl_3): $\delta = 199$, 178.5, 149.7, 131.5, 130.3, 126, 121.3, 114.9, 113.6, 72.0, 52.4, 28.3, 19.5, 19.3.

$\text{C}_{20}\text{H}_{23}\text{NO}_3$ (MW = 325.41); mass spectroscopy (MH^+) 326.

Example A35

Synthesis of N-(3,5-difluorophenyl)alanine *iso*-butyl ester

Following General Procedure AH above and using N-(3,5-difluorophenyl)alanine (from Example AC above) and *iso*-butanol, the title compound was prepared as an oil. The reaction was monitored by tlc on silica gel ($R_f = 0.9$ in 3% methanol/methylene chloride) and purification was by preparative plate chromatography (silica gel using 3% methanol/methylene chloride as the eluant).

NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 6.1$ (m, 3H), 4.5 (bs, 1H), 4.1 (d, 1H), 3.95 (m, 2H), 2.0 (m, 1H), 1.5 (d, $J = 7$ Hz, 3H), 0.95 (d, $J = 6$ Hz, 6H).

^{13}C -nmr (CDCl_3): $\delta = 174.44$, 166.40, 166.19, 163.16, 162.95, 149.43, 96.73, 96.60, 96.48, 96.35, 94.06, 93.72, 93.37, 72.03, 52.30, 28.29, 19.47, 19.23.

$\text{C}_{13}\text{H}_{17}\text{F}_2\text{NO}_2$ (MW = 290.2); mass spectroscopy (MH^+) 291.

Example A36

Synthesis of N-(3,4-dichlorophenyl)alanine O-acetylacetamidoxime ester

Following General Procedure AK above and using N-(3,4-dichlorophenyl)alanine (from Example AB above) and acetamide oxime (prepared according to the procedures described in *J. Org. Chem.*, **46**, 3953 (1981)), the title compound was prepared as a semisolid. The reaction was
5 monitored by tlc on silica gel ($R_f = 0.4$ in ethyl acetate) and purification was by preparative plate chromatography (silica gel using ethyl acetate as the eluant).

NMR data was as follows:

^1H -nmr (DMSO- d_6): $\delta = 7.27$ (d, 1H), 6.81 (s, 1H) 6.4 (broad s, 2H), 6.62 (d, 1H), 6.45 (d, 1H), 4.22 (m, 1H), 1.74 (s, 3H), 1.40 (d, 3H).

10 $\text{C}_{11}\text{H}_{13}\text{Cl}_2\text{N}_3\text{O}_2$ (MW = 290.15); mass spectroscopy (MH^+) 291.

Example A37

Synthesis of N-(3,4-dichlorophenyl)alanine pyrrolyl amide

Following General Procedure AL above and using N-(3,4-dichlorophenyl)alanine (from Example AB above) and pyrrole (Aldrich), the title
15 compound was prepared as an oil. The reaction was monitored by tlc on silica gel ($R_f = 0.28$ in 10% ethyl acetate/hexanes) and purification was by preparative plate chromatography (silica gel using 10% ethyl acetate/hexanes as the eluant).

20 NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 7.36$ (d, $J=2.2$, 2H); 7.20 (d, $J=8.7$, 1H); 6.71 (d, $J=2.7$, 1H); 6.5 (m, 1H); 6.38 (t, $J=2.4$, 2H); 4.8 (m, 1H); 4.57 (d, $J=8.7$, 1H); 1.59 (d, $J=6.8$, 3H).

25 ^{13}C -nmr (CDCl_3): $\delta = 171.9$, 146.1, 133.6, 131.5, 121.9, 119.6, 115.4, 114.7, 113.8, 51.8, 20.2.

$\text{C}_{13}\text{H}_{12}\text{Cl}_2\text{N}_2\text{O}$ (MW = 283); mass spectroscopy (MH^+) 284.

Example A38

Synthesis of N-(3,4-dichlorophenyl)alanine O-acylbutyramideoxime ester

30

Following General Procedure AI above and using N-(3,4-dichlorophenyl)alanine 2,4,6-trichlorophenyl ester (prepared from N-(3,4-

dichlorophenyl)alanine methyl ester (from Example A9) using essentially the same procedure as described in Example AE above) and butyramide oxime (prepared according to the procedures described in *J. Org. Chem.*, **46**, 3953 (1981)), the title compound was prepared as a semisolid. The reaction was monitored by tlc on silica gel ($R_f = 0.25$ in 50% ethyl acetate/hexanes) and purification was by preparative plate chromatography (silica gel using 50% ethyl acetate/hexanes as the eluant).

NMR data was as follows:

^1H -nmr (d_6 -DMSO): $\delta = 7.27$ (d, 1H), 6.83 (s, 1H) 6.38 (broad s, 2H), 6.61 (d, 1H), 6.46 (d, 1H), 4.25 (m, 1H), 2.02 (t, 2H), 1.55 (m, 2H), 1.40 (d, 3H), 0.88 (t, 3H).

$\text{C}_{13}\text{H}_{17}\text{Cl}_2\text{N}_3\text{O}_2$ (MW = 318.20); mass spectroscopy (MH^+) 319.

Example A39

Synthesis of 2-[N-(naphth-2-yl)amino]butanoic acid ethyl ester

Following General Procedure AJ above and using 2-aminonaphthalene (Aldrich) and ethyl 2-bromobutyrate (Aldrich), the title compound was prepared as a solid, m.p. 81-83°C. The reaction was monitored by silica gel tlc ($R_f = 0.5$ in CHCl_3). Purification was by chromatography (silica gel using chloroform as the eluant).

NMR data was as follows: ^1H -nmr (d_6 -DMSO): $\delta = 7.63$ (m, 2H), 7.54 (d, 1H), 7.31 (t, 1H), 7.12 (t, 1H), 7.03 (d, 1H), 6.62 (s, 1H), 6.32 (d, 1H), 4.15 (m, 3H), 1.42 (d, 3H), 1.19 (t, 3H).

$\text{C}_{16}\text{H}_{19}\text{NO}_2$ (MW = 257.34); mass spectroscopy (MH^+) 258.

Example A40

Synthesis of N-(2-naphthyl)alanine *iso*-butyl ester

Following General Procedure AA above and using 2-aminonaphthalene (Aldrich) and *iso*-butyl pyruvate (prepared by following General Procedure AO above), the title compound was prepared as an oil. Purification was by

preparative plate chromatography (silica gel using 25% EtOAc/hexanes as the eluant).

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.65 (m, 3H), 7.38 (t, 1H, J = 6.9 Hz), 7.23 (t, 1H, J = 6.9 Hz), 6.93 (m, 1H), 6.81 (d, 1H, J = 2.3 Hz), 4.31 (q, 1H, J = 6.9 Hz), 3.95 (d, 1H, J = 6.7 Hz), 1.96 (sept, 1H, J = 6.7 Hz), 1.57 (d, 3H, J = 6.9 Hz), 0.93 (dd, 6H, J = 6.7 Hz, J = 1.6 Hz).

¹³C-nmr (CDCl₃) δ = 174.6, 144.2, 134.9, 129.1, 127.8, 127.6, 126.3, 126.0, 122.3, 118.1, 105.3, 71.2, 52.0, 27.7, 18.9, 18.8.

Example A41

Synthesis of N-(2-methylquinolin-6-yl)alanine *iso*-butyl ester

Following General Procedure AA above and using 6-amino-2-methylquinoline (Lancaster) and *iso*-butyl pyruvate (prepared by following General Procedure AO above), the title compound was prepared. The reaction was monitored by silica gel tlc (R_f = 0.44 in 50% EtOAc/hexanes). Purification was by flash chromatography (silica gel using 50% EtOAc/hexanes as the eluant).

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.90 (m, 2H), 7.10 (m, 2H), 6.66 (d, 1H, J = 2.6), 4.50 (bd, 1H), 4.24 (m, 1H), 3.91 (d, 2H, J = 6.6 Hz), 2.64 (s, 3H), 1.91 (sept, 1H, J = 6.7 Hz), 1.52 (d, 3H, J = 6.9 Hz), 0.87 (d, 6H, J = 6.7 Hz).

¹³C-nmr (CDCl₃) δ = 175.0, 155.4, 144.6, 143.4, 134.9, 130.2, 128.4, 122.8, 121.8, 104.9, 71.8, 52.7, 28.3, 25.4, 19.5, 19.4.

C₁₇H₂₂Cl₂N₂O₂ (MW = 286.38); mass spectroscopy (MH⁺) 287.

Example A42

Synthesis of N-(3,4-methylenedioxyphenyl)alanine *iso*-butyl ester

Following reductive amination General Procedure AA above and using 3,4-methylenedioxyaniline (Aldrich) and methyl pyruvate (Aldrich), N-(3,4-

methylenedioxyphenyl)alanine methyl ester was prepared. The methyl ester was then transesterified following General Procedure AQ above and using *iso*-butanol to provide the title compound as an oil. The reaction was monitored by silica gel tlc ($R_f = 0.61$ in 25% EtOAc/hexanes). Purification was by
5 preparative plate chromatography with silica gel using 25% EtOAc/hexanes as the eluant.

NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 6.63$ (d, 1H, 8.3 Hz), 6.25 (d, 1H, $J = 2.3$ Hz), 6.04 (dd, 1H, $J = 8.3$ Hz, $J = 2.3$ Hz), 5.83 (s, 2H), 3.96 (m, 4H), 1.92 (sept, 1H, $J =$
10 6.7 Hz), 1.44 (d, 3H, $J = 6.9$ Hz), 0.90 (d, 6H, $J = 6.6$ Hz).

^{13}C -nmr (CDCl_3): $\delta = 175.4, 148.9, 142.9, 140.8, 109.2, 105.8, 101.2, 97.4, 71.6, 53.6, 28.3, 19.6, 19.5$.

$\text{C}_{14}\text{H}_{19}\text{NO}_4$ (MW = 265.31); mass spectroscopy (MH^+) 265.

15 Example A43

Synthesis of N-(3,4-ethylenedioxyphenyl)alanine *iso*-butyl ester

Following reductive amination General Procedure AA above and using 1,4-benzodioxo-6-amine (Aldrich) and methyl pyruvate (Aldrich), N-(3,4-ethylenedioxyphenyl)alanine methyl ester was prepared. The methyl ester was
20 then transesterified following General Procedure AQ above using *iso*-butanol to provide the title compound. Purification was by preparative plate chromatography.

NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 0.91$ (d, $J = 7\text{Hz}$, 6H), 1.42 (d, $J = 7\text{Hz}$, 3H), 1.8-2.0 (m, 1H), 3.8-3.95 (m, 3H), 4.0-4.1 (m, 1H), 4.15-4.25 (m, 4H), 6.12-6.2 (m, 2H), 6.65-6.75 (m, 1H).

^{13}C -nmr (CDCl_3): $\delta = 19.55, 19.56, 19.67, 28.3, 53.4, 64.7, 65.3, 71.7, 103.1, 108.0, 118.3, 142.1, 144.6, 175.4$.

$\text{C}_{15}\text{H}_{21}\text{NO}_4$ (MW = 279.34); mass spectroscopy (MH^+) 280.

Example A44

Synthesis of N-(2-naphthyl)alanine methyl ester

Following reductive amination General Procedure AA above and using 2-aminonaphthalene (Aldrich) and methyl pyruvate (Aldrich), the title compound was prepared. The reaction was monitored by silica gel tlc ($R_f = 0.50$ in 25% EtOAc/hexanes). Purification was by flash chromatography with silica gel using 25% EtOAc/hexanes as the eluant.

NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 7.65$ (m, 3H), 7.48 (m, 1H), 7.25 (m, 1H), 6.91 (m, 1H), 6.79 (m, 1H), 4.31 (m, 2H), 3.76 (s, 3H), 1.55 (d, 3H).

^{13}C -nmr (CDCl_3): $\delta = 175.66$, 144.78, 135.55, 129.78, 128.47, 128.22, 126.96, 126.67, 123.01, 118.66, 105.88, 52.95, 52.51, 19.45.

$\text{C}_{14}\text{H}_{15}\text{NO}_2$ (MW = 229.28); mass spectroscopy (MH^+) 229.

Example A45

Synthesis of N-(benzothiazol-6-yl)alanine ethyl ester

To a solution of 6-aminobenzothiazole (Lancaster) in dichloromethane was added 1.2 equivalents of pyridine, followed by 1.5 equivalents of trifluoroacetic anhydride. The reaction was stirred at room temperature for 3 hours and then washed with 5% citric acid, dried over MgSO_4 , and stripped free of solvent on a rotary evaporator to yield 6-trifluoroacetamidothiazole. This material was dissolved in THF and then added to a suspension of KH in THF at 0°C . A catalytic amount of 18-crown-6 was added, followed by ethyl 2-bromopropionate (Aldrich). The reaction was held at room temperature for 1 hour, and then heated to reflux for 24 hours, and then cooled to room temperature. The reaction mixture was stripped free of solvent on a rotary evaporator and the resulting residue was dissolved in ether. This solution was washed with water, saturated aqueous NaCl, and dried over MgSO_4 . The solution was stripped free of solvent on a rotary evaporator and the title compound was obtained by chromatography of the residue using 5% methanol/dichloromethane ($R_f = 0.59$) as the eluant.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 8.69 (s, 1H), 7.90 (d, 1H, J = 8.8 Hz), 7.04 (d, 1H, J = 2.3 Hz), 6.84 (dd, 1H, J = 8.8 Hz, J = 2.4 Hz), 4.41 (bd, 1H, J = 7.5 Hz), 4.20 (m, 3H), 1.53 (d, 3H, J = 6.9 Hz), 1.27 (t, 3H, J = 7.1 Hz).

5 ¹³C-nmr (CDCl₃): δ = 174.9, 150.2, 147.1, 145.6, 136.3, 124.6, 115.7, 103.5, 61.9, 52.9, 19.4, 14.8.

C₁₂H₁₄N₂O₂S (MW = 250.32); mass spectroscopy (MH⁺) 251.

Example A46

10 **Synthesis of N-(indol-5-yl)alanine *iso*-butyl ester (S isomer)**

Following General Procedure AM and using 5-aminoindole (Aldrich) and *iso*-butyl R-(+)-lactate (Aldrich), the title compound was prepared as an oil.

The reaction was monitored by silica gel tlc (R_f = 0.46 in 33% EtOAc/hexanes).

15 Purification was by preparative plate chromatography with silica gel using 33% EtOAc/hexanes as the eluant.

NMR data was as follows:

20 ¹H-nmr (CDCl₃): δ = 8.11 (bs, 1H), 7.07 (d, J=8.8 Hz, 1H), 6.98 (d, J=2.8 Hz, 1H), 6.83 (d, J=2.2 Hz, 1H), 6.61 (m, 1H), 6.32 (m, 1H), 4.18 (q, J=6.9 Hz, 1H), 3.95 (bs, 1H), 3.87 (d, J=6.7 Hz, 2H), 1.89 (hept, J=6.7 Hz, 1H), 1.48 (d, J=6.96 Hz, 3H), 0.86 (dd, J=6.7 Hz, J=1.6 Hz, 6H).

¹³C-nmr (CDCl₃): δ = 176.15, 141.06, 131.28, 129.24, 125.34, 113.34, 112.53, 104.21, 102.17, 71.65, 54.28, 28.36, 19.87, 19.62.

C₁₅H₂₀N₂O₂ (MW = 260.34); mass spectroscopy (MH⁺) 261.

25

Example A47

Synthesis of N-(naphth-2-yl)alanine O-acetylacetamidoxime ester

Following General Procedure AI above using N-(naphth-2-yl)alanine 2,4,6-trichlorophenyl ester (from Example AE above) and acetamide oxime (prepared according to the procedures described in *J. Org. Chem.*, **46**, 3953 (1981)), the title compound was prepared as a semisolid. The reaction was monitored by tlc

30

on silica gel ($R_f = 0.4$ in ethyl acetate) and purification was by preparative plate chromatography (silica gel using ethyl acetate as the eluant).

NMR data was as follows:

^1H -nmr (d_6 -DMSO): $\delta = 7.64$ (t, 2H), 7.54 (d, 1H), 7.32 (t, 1H), 7.13 (t, 1H),
5 7.04 (d, 1H), 6.78 (s, 1H) 6.42 (broad s, 2H), 6.32 (d, 1H), 4.33 (m, 1H), 1.72
(s, 3H), 1.46 (d, 3H).

$\text{C}_{15}\text{H}_{17}\text{N}_3\text{O}_2$ (MW = 271.32); mass spectroscopy: 271.

Example A48

10

Synthesis of N-(2-naphthyl)alanine ethyl ester

Following reductive amination General Procedure AA above and using 2-aminonaphthalene (Aldrich) and ethyl pyruvate (Aldrich), the title compound
was prepared as a solid having a melting point of 52-56°C. The reaction was
15 monitored by silica gel tlc ($R_f = 0.50$ in 25% EtOAc/hexanes). Purification was
by flash chromatography with silica gel using 25% EtOAc/hexanes as the eluant.

NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 7.65$ (m, 3H), 7.48 (m, 1H), 7.25 (m, 1H), 6.91 (m,
1H), 6.79 (m, 1H), 4.31 (m, 2H), 3.76 (s, 3H), 1.55 (d, 3H).

20 ^{13}C -nmr (CDCl_3): $\delta = 175.66, 144.78, 135.55, 129.78, 128.47, 128.22,$
126.96, 126.67, 123.01, 118.66, 105.88, 52.95, 52.51, 19.45.

$\text{C}_{14}\text{H}_{15}\text{NO}_2$ (MW = 229.28); mass spectroscopy (MH^+) 229.

Example A49

25

Synthesis of N-(3,4-dichlorophenyl)alanine O-acylpropionamidoxime ester

Following General Procedure AI above using N-(3,4-dichlorophenyl)alanine
2,4,6-trichlorophenyl ester (prepared from N-(3,4-dichlorophenyl)alanine methyl
ester (from Example A9) using essentially the same procedure as described in
Example AE above) and propionamide oxime (prepared according to the
30 procedures described in *J. Org. Chem.*, 46, 3953 (1981)), the title compound
was prepared as a semisolid. The reaction was monitored by tlc on silica gel

(R_f = 0.2 in 50% ethyl acetate/hexane) and purification was by preparative plate chromatography (silica gel using 50% ethyl acetate/hexane as the eluant).

NMR data was as follows:

^1H -nmr (d_6 -DMSO): δ = 7.27 (d, 1H), 6.83 (s, 1H), 6.64 (d, 1H), 6.47 (d, 1H), 6.38 (broad s, 2H), 4.24 (m, 1H), 2.07 (q, 2H), 1.41 (d, 3H).

$\text{C}_{12}\text{H}_{15}\text{Cl}_2\text{N}_3\text{O}_2$ (MW = 304.17); mass spectroscopy (MH^+) 305.

Example A50

Synthesis of N-(4-ethoxycarbonylphenyl)alanine *iso*-butyl ester (S isomer)

Following General Procedure AM and using ethyl 4-aminobenzoate (Aldrich) and *iso*-butyl R-(+)-lactate (Aldrich), the title compound was prepared as an oil. The reaction was monitored by silica gel tlc (R_f = 0.21 in 10% EtOAc/hexanes). Purification was by preparative plate thin layer chromatography using 25% EtOAc/hexanes as the eluant.

NMR data was as follows:

^1H -nmr (CDCl_3): δ = 7.82 (d, J = 8.73 Hz, 2H), 6.51 (d, J = 8.79 Hz, 2H), 4.81 (d, J = 7.82 Hz, 1H), 4.25 (q, J = 7.14 Hz, 2H), 4.15 (quint, J = 7.40 Hz, 1H), 3.87 (m, 2H), 1.87 (sept, J = 6.70 Hz, 1H), 1.43 (d, J = 6.95 Hz, 3H), 1.30 (t, J = 7.14 Hz, 3H), 0.84 (d, J = 6.71 Hz, 6H).

^{13}C -nmr (CDCl_3): δ = 174.5, 167.3, 151.0, 132.0, 119.9, 112.5, 71.9, 60.8, 51.9, 28.2, 19.5, 19.2, 15.0.

$\text{C}_{16}\text{H}_{23}\text{NO}_4$ (MW = 293.37); mass spectroscopy (MH^+) 294.

Example A51

Synthesis of N-[3,5-di(trifluoromethyl)phenyl]alanine *iso*-butyl ester (S isomer)

Following General Procedure AM and using 3,5-di(trifluoromethyl)aniline (Aldrich) and *iso*-butyl R-(+)-lactate (Aldrich), the title compound was prepared as an oil. The reaction was monitored by silica gel tlc (R_f = 0.38 in 10% EtOAc/hexanes). Purification was by preparative plate thin layer chromatography using 10% EtOAc/hexanes as the eluant.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.13 (s, 1H), 6.91 (s, 2H), 4.97 (d, J = 8.24 Hz, 1H), 4.18 (m, 1H), 3.93 (d, J = 6.59 Hz, 2H), 1.93 (sept, J = 6.71 Hz, 1H), 1.49 (d, J = 7.02 Hz, 3H), 0.89 (d, J = 6.59 Hz, 6H).

5 ¹³C-nmr (CDCl₃): δ = 174.4, 147.9, 133.6, 133.2, 132.7, 132.3, 129.4, 125.8, 122.2, 118.6, 112.81, 112.76, 111.42, 111.37, 111.32, 111.27, 111.22, 72.2, 52.0, 32.1, 28.24, 28.17, 23.2, 19.5, 19.3, 19.2, 18.9, 14.6.

C₁₅H₁₇F₆NO₂ (MW = 357.30); mass spectroscopy (MH⁺) 358.

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Example A52

Synthesis of N-(3,5-dimethoxyphenyl)alanine *iso*-butyl ester

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N-(3,5-dimethoxyphenyl)alanine (crude, 454 mg) (prepared according to the procedure described in U.S. Patent No. 3,598,859 using 3,5-dimethoxyaniline (Aldrich) and 2-chloropropionic acid (Aldrich)) was treated in dry *iso*-butanol (10 mL) with 0.1 mL of chlorotrimethylsilane and the reaction mixture refluxed overnight. The excess alcohol was removed at reduced pressure and the residue dissolved in ethyl acetate. The ethyl acetate solution was washed with saturated aqueous NaHCO₃, dried with Na₂SO₄ and the solvent removed to provide the title compound. The reaction was monitored by silica gel tlc (R_f = 0.3 in 20% EtOAc/hexanes). Purification was by preparative thin layer chromatography using 20% EtOAc/hexanes as the eluant.

20

NMR data was as follows:

25

¹H-nmr (CDCl₃): δ = 0.9 (d, J = 7, 6H), 1.47 (d, J = 7, 3H), 1.9-2.0 (m, 1H), 3.7 (s, 6H), 3.85-4.0 (m, 2H), 4.1-4.2 (m, 1H), 4.3 (brs, 1H), 5.8 (s, 2H), 5.9 (s, 1H).

¹³C-nmr (CDCl₃): δ = 19.49, 19.52, 19.54, 28.3, 52.5, 55.6, 71.7, 91.1, 92.7, 149.2, 162.3, 175.2.

30

C₁₅H₂₃NO₄ (MW = 281.35).

Example A53

Synthesis of N-(2-naphthyl)alanine O-acylpropionamidoxime ester

Following General Procedure AS and using N-(2-naphthyl)alanine 2,4,5-trichlorophenyl ester (from Example AE above) and propionamide oxime (prepared according to the procedures described in *J. Org. Chem.*, **46**, 3953 (1981)), the title compound was prepared. The reaction was monitored by silica gel tlc ($R_f = 0.5$ in EtOAc). Purification was by silica gel chromatography using 1:1 EtOAc/hexanes as the eluant.

NMR data was as follows:

^1H -nmr (DMSO- d_6): $\delta = 1.03$ (t, 3H), 1.45 (d, 3H).

$\text{C}_{16}\text{H}_{19}\text{N}_3\text{O}_2$ (MW = 285.35); mass spectroscopy (M^+) 285.

Example A54

Synthesis of N-(2-naphthyl)alanine O-acylbutyramidoxime ester

Following General Procedure AS and using N-(2-naphthyl)alanine 2,4,5-trichlorophenyl ester (from Example AE above) and butyramide oxime (prepared according to the procedures described in *J. Org. Chem.*, **46**, 3953 (1981)), the title compound was prepared as an oil. The reaction was monitored by silica gel tlc ($R_f = 0.6$ in EtOAc). Purification was by silica gel chromatography using 1:1 EtOAc/hexanes as the eluant.

NMR data was as follows:

^1H -nmr (DMSO- d_6): $\delta = 0.86$ (t, 3H), 1.46 (d, 3H).

$\text{C}_{17}\text{H}_{21}\text{N}_3\text{O}_2$ (MW = 299.37); mass spectroscopy (MH^+) 299.

Example A55

Synthesis of N-(2-naphthyl)alanine O-acylisovaleramidoxime ester

Following General Procedure AS and using N-(2-naphthyl)alanine 2,4,5-trichlorophenyl ester (from Example AE above) and isovaleramide oxime (prepared according to the procedures described in *J. Org. Chem.*, **46**, 3953 (1981)), the title compound was prepared as an oil. The reaction was monitored

by silica gel tlc ($R_f = 0.3$ in 1:1 EtOAc/hexanes). Purification was by silica gel chromatography using 1:1 EtOAc/hexanes as the eluant.

NMR data was as follows:

^1H -nmr (DMSO- d_6): $\delta = 0.86$ (t, 3H), 1.45 (d, 3H).

5 $\text{C}_{18}\text{H}_{23}\text{N}_3\text{O}_2$ (MW = 313.40); mass spectroscopy (MH^+) 313.

Example A56

Synthesis of N-(2-naphthyl)alanine O-acylbenzamidoxime ester

10 Following General Procedure AS and using N-(2-naphthyl)alanine 2,4,5-trichlorophenyl ester (from Example AE above) and benzamide oxime (prepared according to the procedures described in *J. Org. Chem.*, **46**, 3953 (1981)), the title compound was prepared as an oil. The reaction was monitored by silica gel tlc ($R_f = 0.3$ in 1:1 EtOAc/hexanes). Purification was by silica gel
15 chromatography using 1:1 EtOAc/hexanes as the eluant.

NMR data was as follows:

^1H -nmr (DMSO- d_6): $\delta = 4.42$ (m, 1H), 1.53 (d, 3H).

$\text{C}_{20}\text{H}_{19}\text{N}_3\text{O}_2$ (MW = 333.39); mass spectroscopy (MH^+) 333.

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Example A57

Synthesis of N-(2-naphthyl)alanine O-acylcyclopropanecarboxamidoxime ester

25 Following General Procedure AS and using N-(2-naphthyl)alanine 2,4,5-trichlorophenyl ester (from Example AE above) and cyclopropanecarboxamide oxime (prepared according to the procedures described in *J. Org. Chem.*, **46**, 3953 (1981)), the title compound was prepared as an oil. The reaction was monitored by silica gel tlc ($R_f = 0.3$ in 1:1 EtOAc/hexanes). Purification was by silica gel chromatography using 1:1 EtOAc/hexanes as the eluant.

30

NMR data was as follows:

^1H -nmr (DMSO- d_6): $\delta = 0.85$ (m, 4H), 1.43 (d, 3H).

$\text{C}_{17}\text{H}_{19}\text{N}_3\text{O}_2$ (MW = 297.36); mass spectroscopy (MH^+) 297.

Example A58

Synthesis of N-(2-naphthyl)alanine O-acylcyclopropylacetamidoxime ester

Following General Procedure AS and using N-(2-naphthyl)alanine 2,4,5-trichlorophenyl ester (from Example AE above) and cyclopropylacetamidoxime (prepared according to the procedures described in *J. Org. Chem.*, **46**, 3953 (1981)), the title compound was prepared as an oil. The reaction was monitored by silica gel tlc ($R_f = 0.3$ in 1:1 EtOAc/hexanes). Purification was by silica gel chromatography using 1:1 EtOAc/hexanes as the eluant.

NMR data was as follows:

^1H -nmr (DMSO- d_6): $\delta = 1.43$ (d, 3H), 1.91 (d, 2H).

$\text{C}_{18}\text{H}_{21}\text{N}_3\text{O}_2$ (MW = 311.39); mass spectroscopy (MH^+) 311.

Example A59

Synthesis of N-(2-naphthyl)alanine O-acylcyclopentanecarboxamidoxime ester

Following General Procedure AS and using N-(2-naphthyl)alanine 2,4,5-trichlorophenyl ester (from Example AE above) and cyclopentanecarboxamidoxime (prepared according to the procedures described in *J. Org. Chem.*, **46**, 3953 (1981)), the title compound was prepared as an oil. The reaction was monitored by silica gel tlc ($R_f = 0.3$ in 1:1 EtOAc/hexanes). Purification was by silica gel chromatography using 1:1 EtOAc/hexanes as the eluant.

NMR data was as follows:

^1H -nmr (DMSO- d_6): $\delta = 1.43$ (d, 3H), 2.43 (m, 1H).

$\text{C}_{17}\text{H}_{19}\text{N}_3\text{O}_2$ (MW = 297.36).

GENERAL PROCEDURE BA

Coupling of $\text{R}^1\text{C}(\text{X}')(\text{X}'')\text{C}(\text{O})\text{Cl}$ with $\text{H}_2\text{NCH}(\text{R}^2)\text{C}(\text{O})\text{XR}^3$

To a stirred solution of (D,L)-alanine *iso*-butyl ester hydrochloride (from Example BB below) (4.6 mmol) in 5 mL of pyridine was added 4.6 mmol of an acid chloride. Precipitation occurred immediately. The mixture was stirred for

3.5 h, diluted with 100 mL of diethyl ether, washed with 10% HCl three times, brine once, 20% potassium carbonate once and brine once. The solution was dried over magnesium sulfate, filtered, and evaporated at reduced pressure to yield the product. Other amino acid esters may also be employed in this procedure.

GENERAL PROCEDURE BB

Coupling of $R^1C(X')(X'')C(O)OH$ with $H_2NCH(R^2)C(O)XR^3$

A solution of the acid (3.3 mmol) and CDI in 20 mL THF was stirred for 2 h. L-alanine *iso*-butyl ester hydrochloride (from Example BB below) (3.6 mmol) was added, followed by 1.5 mL (10.8 mmol) of triethylamine. The reaction mixture was stirred overnight. The reaction mixture was diluted with 100 mL of diethyl ether, washed with 10% HCl three times, brine once, 20% potassium carbonate once and brine once. The solution was dried over magnesium sulfate, filtered, and evaporated at reduced pressure to yield the product. Other amino acid esters may also be employed in this procedure.

GENERAL PROCEDURE BC

Esterification of $R^1C(X')(X'')C(O)NHCH(R^2)C(O)OH$ With HOR^3

To a stirred solution of phenylacetylvaline (1.6470 g, 7.0 mmol) in 20 mL THF was added CDI (1.05 g, 6.5 mmol) and the mixture was stirred for 1.5 h. 2-Methylbutanol (0.53 g, 6 mmol) was added the mixture, followed by addition of NaH (0.16 g, 6.5 mmol). Bubbling occurred immediately. The reaction mixture was stirred overnight. The reaction mixture was diluted with 100 mL of diethyl ether, washed with 10% HCl three times, brine once, 20% potassium carbonate once and brine once. The solution was dried over magnesium sulfate, filtered, and evaporated at reduced pressure to yield the product. Other N-acyl amino acids and alcohols may also be employed in this procedure.

GENERAL PROCEDURE BD

Ester Hydrolysis to the Free Acid

Ester hydrolysis to the free acid was conducted by conventional methods. Below are two examples of such conventional de-esterification methods.

To the ester in a 1:1 mixture of $\text{CH}_3\text{OH}/\text{H}_2\text{O}$ was added 2-5 equivalents of
5 K_2CO_3 . The mixture was heated to about 50°C for about 0.5 to 1.5 hours until
tlc showed complete reaction. The reaction was cooled to room temperature and
the methanol was removed at reduced pressure. The pH of the remaining
aqueous solution was adjusted to about 2, and ethyl acetate was added to extract
the product. The organic phase was then washed with saturated aqueous NaCl
10 and dried over MgSO_4 . The solution was stripped free of solvent at reduced
pressure to yield the product.

The amino acid ester was dissolved in dioxane/water (4:1) to which was
added LiOH (~2 eq.) that was dissolved in water such that the total solvent after
15 addition was about 2:1 dioxane:water. The reaction mixture was stirred until
reaction completion and the dioxane was removed under reduced pressure. The
residue was diluted with EtOAc , the layers were separated and the aqueous layer
acidified to pH 2. The aqueous layer was back extracted with EtOAc , the
combined organics were dried over Na_2SO_4 and the solvent was removed under
20 reduced pressure after filtration. The residue was purified by conventional
methods (e.g., recrystallization).

The following exemplifies this later example. The methyl ester of 3- NO_2
phenylacetyl alanine 9.27 g (0.0348 mols) was dissolved in 60 mL dioxane and
25 15 mL of H_2O and adding LiOH (3.06 g, 0.0731 mol) that has been dissolved in
15 mL of H_2O . After stirring for 4 hours, the dioxane was removed under
reduced pressure and the residue diluted with EtOAc , the layers were separated
and the aqueous layer acidified to pH 2. The aqueous layer was back extracted
with EtOAc (4 X 100 mL), the combined organics were dried over Na_2SO_4 and
30 the solvent was removed under reduced pressure after filtration. The residue
was recrystallized from EtOAc /isooctane giving 7.5 g (85%) of 3-

nitrophenylacetyl alanine. $C_{11}H_{12}N_2O_5$ requires C = 52.38, H = 4.80, and N = 11.11. Analysis found C = 52.54, H = 4.85, and N = 11.08. $[\alpha]_{23} = -29.9$ @ 589 nm.

5

GENERAL PROCEDURE BE

Low Temperature BOP Coupling of Acid and Alcohol

A solution of methylene chloride containing the carboxylic acid (100M%) and N-methyl morpholine (150 M%) was cooled to -20°C under nitrogen. BOP (105 M%) was added in one portion and the reaction mixture was maintained at
10 -20°C for 15 minutes. The corresponding alcohol (120 M%) was added and the reaction mixture was allowed to warm to room temperature and stirred for 12 hours. The reaction mixture was then poured into water and extracted with ethyl acetate (3x). The combined ethyl acetate portions were backwashed with saturated aqueous citric acid (2x), saturated aqueous sodium bicarbonate (2x),
15 brine (1x), dried over anhydrous magnesium sulfate or sodium sulfate and the solvent removed under reduced pressure to yield the crude product.

GENERAL PROCEDURE BF

EDC Coupling of Acid and Amine

20 The acid derivative was dissolved in methylene chloride. The amine (1 eq.), N-methylmorpholine (5 eq.), and hydroxybenzotriazole monohydrate (1.2 eq.) were added in sequence. The reaction was cooled to about 0°C and then 1.2 eq. of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride was added. The solution was allowed to stir overnight and come to room
25 temperature under N_2 pressure. The reaction mix was worked up by washing the solution with saturated, aqueous Na_2CO_3 , 0.1M citric acid, and brine before drying with Na_2SO_4 and removal of solvents to yield crude product. Pure products were obtained by flash chromatography in an appropriate solvent.

30

GENERAL PROCEDURE BG

EDC Coupling of Acid and Amine

A round bottom flask was charged with carboxylic acid (1.0 eq.), hydroxy-benzotriazole hydrate (1.1 eq.) and amine (1.0 eq.) in THF under nitrogen atmosphere. An appropriate amount (1.1 eq. for free amines and 2.2 eq. for hydrochloride amine salts) of base, such as Hunig's base was added to the well stirred mixture followed by EDC (1.1 eq.). After stirring from 4 to 17 hours at room temperature the solvent was removed at reduced pressure, the residue taken up in EtOAc (or similar solvent)/water. The organic layer was washed with saturated aqueous sodium bicarbonate solution, 1N HCl, brine and dried over anhydrous sodium sulfate. In some cases, the isolated product was analytically pure at this stage while, in other cases, purification via chromatography and/or recrystallization was required prior to biological evaluation.

GENERAL PROCEDURE BH

Coupling of $R^1C(X')(X'')C(O)Cl$ with $H_2NCH(R^2)C(O)XR^3$

An excess of oxalyl chloride in dichloromethane was added to the acid derivative together with one drop of DMF. The resulting mixture was stirred for about 2 hours or until bubbling ceases. The solvent was then removed under reduced pressure and rediluted with dry methylene chloride. To the resulting solution was added about 1.1 eq. of the appropriate amino acid ester and triethylamine (1.1 eq. in methylene chloride). The system was stirred at room temperature for 2 hours and then the solvent was removed under reduced pressure. The residue was dissolved in ethyl acetate, washed with 1N HCl followed by 1N NaOH. The organic layer was dried over anhydrous sodium sulfate, filtered and the solvent removed under reduced pressure to provide for the desired product.

GENERAL PROCEDURE BI

P-EPC coupling

P-EPC coupling employs an amino acid ester and a substituted acetic acid compound. The acetic acid derivative is well known in the art and is typically

Specifically, the appropriate amino ester free base (0.0346 mmols) and substituted phenylacetic acid (0.069 mmols) were dissolved in 2.0 mL CHCl_3 (EtOH free), treated with 150 mg of P-EPC (0.87 meq./g) and the reaction was mixed for 4 days at 23°C. The reaction was filtered through a plug of cotton, rinsed with 2.0 mL of CHCl_3 and the filtrate evaporated under a stream of nitrogen. The purity of each sample was determined by ^1H NMR and ranged from 50% to >95%. Between 8.0 and 15.0 mg of final product was obtained from each reaction and was tested without additional purification.

Synthesis of Amino Acid Esters From the Corresponding N-BOC Amino Acid

The N-BOC amino acid was dissolved in dioxane and treated with an excess of alcohol (~1.5 eq.) and catalytic DMAP (100 mg) at 0°C. Stirring was continued until reaction completion whereupon the product was recovered by conventional methods.

The N-BOC protected amino acid was dissolved in methylene chloride (0.05M) and treated with 10 eq. of TFA at room temperature under a nitrogen atmosphere. The reaction was monitored by tlc until starting material was consumed usually within 1-5 hours. An additional 10 eq. of TFA was added to the reaction if the starting material was still present after 5 hours. The reaction was carefully neutralized with Na_2CO_3 , separated, the organic layer washed with brine and dried over anhydrous Na_2SO_4 . The crude amine was then used without purification.

Specific exemplification of these procedures are as follows:

1. Racemic (+/-)-N-BOC- α -amino butyric acid (Aldrich) (9.29 g, 0.0457 mol) was dissolved in 100 mL of dioxane and treated with *iso*-butyl alcohol (6.26 mL, 0.0686 mol), EDC (8.72 g, 0.0457) and catalytic DMAP (100 mg) at 0°C. After stirring for 17 hours, the organics were evaporated at reduced pressure, the residue diluted with EtOAc washed with NaHCO₃, brine and dried over Na₂SO₄. Evaporation yields 8.42 g (71%) of an oil. C₁₃H₂₅NO₄ requires: C = 60.21, H = 9.72, and N = 5.40. Anal found: C = 59.91, H = 9.89, and N = 5.67.

The above N-BOC amino acid ester (8.00 g, 0.032 mol) was deprotected as above giving 3.12 g (61%) of the free base as a colorless oil which solidifies upon standing.

2. L-N-BOC-alanine (Aldrich) (8.97 g, 0.047 mol) was dissolved in 100 mL of CH₂Cl₂, *iso*-butyl alcohol (21.9 mL, 0.238 mol) and treated with DMAP (100 mg) and EDC (10.0 g, 0.52 mol) at 0°C. The mixture was stirred for 17 hours, diluted with H₂O, washed with 1.0 N HCl, NaHCO₃, then brine and the organics were dried over Na₂SO₄. Filtration and evaporation yields 11.8 g (quantitative) of L-N-BOC alanine *iso*-butyl ester which is contaminated with a small amount of solvent. A sample was vacuum dried for analytical analysis. C₁₂H₂₃NO₄ requires: C = 58.79, H = 9.38, and N = 5.71. Anal found: C = 58.73, H = 9.55, and N = 5.96.

The above N-BOC amino acid ester (11.8 g, 0.0481 mol) was deprotected as above. The free base was converted to the corresponding HCl salt using saturated HCl (g)/EtOAc to give L-N-alanine *iso*-butyl ester hydrochloride. Obtained 4.2 g (48%) of a colorless solid. C₇H₁₅NO₂. HCl requires: C = 46.28, H = 8.88, and N = 7.71. Anal found: C = 46.01, H = 8.85, and N = 7.68.

GENERAL PROCEDURE BK

Methyl ester formation from amino acids

The amino acid (amino acid or amino acid hydrochloride) is suspended in methanol and chilled to 0°C. HCl gas is bubbled through this solution for 5 minutes. The reaction is allowed to warm to room temperature then stirred for 4 hours. The solvents are then removed at reduced pressure to afford the desired amino acid methyl ester hydrochloride. This product is usually used without further purification.

Example BA

Synthesis of free and polymer bound PEPC

N-ethyl-N'-3-(1-pyrrolidiny)propylurea

To a solution of 27.7 g (0.39 mol) ethyl isocyanate in 250 mL chloroform was added 50 g (0.39 mol) 3-(1-pyrrolidiny)propylamine dropwise with cooling. Once the addition was complete, the cooling bath was removed and the reaction mixture stirred at room temperature for 4 hours. The reaction mixture was then concentrated under reduced pressure to give 74.5 g (96.4%) of the desired urea as a clear oil.

1-(3-(1-pyrrolidiny)propyl)-3-ethylcarbodiimide (P-EPC)

To a solution of 31.0 g (0.156 mol) N-ethyl-N'-3-(1-pyrrolidiny)propylurea in 500 mL dichloromethane was added 62.6 g (0.62 mol) triethylamine and the solution was cooled to 0°C. To this solution were then added 59.17 g (0.31 mol) 4-toluenesulfonyl chloride in 400 mL dichloromethane dropwise at such a rate as to maintain the reaction at 0-5°C. After the addition was complete, the reaction mixture was warmed to room temperature and then heated to reflux for 4 hours. After cooling to room temperature, the reaction mixture was washed with saturated aqueous potassium carbonate (3 x 150 mL). The aqueous phases were combined and extracted with dichloromethane. All

organic phases were combined and concentrated under reduced pressure. The resultant orange slurry was suspended in 250 mL diethyl ether and the solution decanted off from the solid. The slurry/decantation process was repeated 3 more times. The ether solutions were combined and concentrated under reduced pressure to give 18.9 g (67%) of the desired product as a crude orange oil. A portion of the oil was distilled under vacuum to give a colorless oil distilling at 78-82°C (0.4 mm Hg).

10 Preparation of a polymer supported form of 1-(3-(1-pyrrolidinyl)propyl)-3-ethylcarbodiimide (P-EPC)

A suspension of 8.75 g (48.3 mmol) 1-(3-(1-pyrrolidin-yl)propyl)-3-ethylcarbodiimide and 24.17 g (24.17 mmol) Merrifield's resin (2% cross-linked, 200-400 mesh, chloromethylated styrene/divinylbenzene copolymer, 1 meq. Cl/g) in dimethylformamide was heated at 100°C for 2 days. The reaction was cooled and filtered and the resulting resin washed sequentially with 1L DMF, 1L THF and 1L diethyl ether. The remaining resin was then dried under vacuum for 18 hours.

Example BB

20 **Preparation of alanine *iso*-butyl ester hydrochloride**

A mixture of 35.64 g (0.4 mol) of (D,L)-alanine (Aldrich) (or L-alanine (Aldrich)); 44 mL (0.6 mol) of thionyl chloride (Aldrich) and 200 mL of isobutanol was refluxed for 1.5 hours and the volatiles were removed completely on a rotavapor of 90°C under reduced pressure to give (D,L)-alanine *iso*-butyl ester hydrochloride (or L-alanine *iso*-butyl ester hydrochloride), which was pure enough to be used for further transformations.

Example BC

Preparation of 3,5-dichlorophenylacetic acid

30 To a solution of 3.5 g of 3,5-dichlorobenzyl alcohol (Aldrich) in 75 mL of dichloromethane at 0°C was added 1.8 mL of methane sulfonylchloride

followed by 3.5 mL of triethylamine added dropwise. After 2 hours the solution was diluted to 150 mL with dichloromethane, washed with 3N HCl, saturated aqueous NaHCO₃ dried with Na₂SO₄ and the solvents removed to yield the desired 3,5-dichlorobenzyl methanesulfonate as a yellow oil that was used without purification.

The crude sulfonate was dissolved in 50 mL of DMF at 0°C and then 3 g of KCN was added. After 2 hours an additional 50 mL of DMF was added and the solution was stirred for 16 hours. The red solution was diluted with 1 L of H₂O and acidified to pH 3 with 3N HCl. The aqueous solution was extracted with dichloromethane. The combined organics were washed with 3N HCl, dried with Na₂SO₄ and the solvents removed at reduced pressure to yield crude 3,5-dichlorophenylacetonitrile which was used without purification.

The nitrile was added to a mixture of 40 mL of concentrated sulfuric acid and 50 mL H₂O and heated to reflux for 48 hours, cooled to room temperature and stirred for 48 hours. The reaction was diluted into 1 L of crushed ice, warmed to room temperature and extracted with 2 x 200 mL of dichloromethane and 2 x 200 mL of ethylacetate. Both sets of organics were combined and washed with saturated aqueous NaHCO₃. The NaHCO₃ fractions were combined and acidified to pH 1 with 3N HCl. The white solid was too fine to filter and was extracted out with 2 X 200 mL of dichloromethane. The combined organics were dried with Na₂SO₄ and the solvents removed at reduced pressure to yield crude 3,5-dichlorophenylacetic acid as a white solid. The solid was slurried with hexane and filtered to get 1.75g of white solid.

NMR (CDCl₃): (in ppm) 3.61 (s, 2H), 7.19 (s, 1H), 7.30 (s, 1H)

Example BD

Synthesis of N-(3-chlorophenylacetyl)alanine

The title compound was prepared using L-alanine (Nova Biochem) and 3-chlorophenyl acetic acid (Aldrich) by following General Procedures BF or BG, followed by hydrolysis using General Procedure BD.

Example B1

Synthesis of N-(phenylacetyl)-D,L-alanine *iso*-butyl ester

Following General Procedure BA above and using phenylacetyl chloride (Aldrich) and D,L-alanine *iso*-butyl ester hydrochloride (from Example BB above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by extraction with Et₂O followed by washes with aqueous K₂CO₃ and aqueous HCl.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.23-7.36 (m, 5H), 6.18 (d, 1H), 4.58 (t, *J* = 7.3 Hz, 1H), 3.87 (m, 2H), 3.57 (s, 2H), 1.90 (m, 1H), 1.34 (d, *J* = 7.2 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 6H).

¹³C-nmr (CDCl₃): δ = 172.7, 170.3, 134.5, 129.2, 128.8, 127.2, 71.3, 48.1, 43.4, 27.5, 18.8, 18.3.

C₁₅H₂₁NO₃ (MW = 263.34; Mass Spectroscopy (MH⁺ = 264))

Example B2

Synthesis of N-(3-phenylpropionyl)-D,L-alanine *iso*-butyl ester

Following General Procedure BA above and using 3-phenylpropionyl chloride (Aldrich) and D,L-alanine *iso*-butyl ester hydrochloride (from Example BB above), the title compound was prepared as a solid having a melting point of from 51°-54°C. The reaction was monitored by tlc on silica gel and purification was by extraction with Et₂O followed by washes with aqueous K₂CO₃ and aqueous HCl.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.25 (m, 2H), 7.19 (m, 3H), 6.28 (d, *J* = 7.2 Hz, 1H), 4.58 (quint., *J* = 7.2 Hz, 1H), 3.89 (m, 2H), 2.95 (t, *J* = 7.7 Hz, 2H), 2.50 (m, 2H), 1.92 (m, 1H), 1.33 (d, *J* = 7.1 Hz, 3H), 0.91 (d, *J* = 6.7 Hz, 6H).

¹³C-nmr (CDCl₃): δ = 173.0, 171.5, 140.6, 128.3, 128.1, 126.0, 71.2, 47.8, 37.9, 31.4, 27.5, 18.79, 18.77, 18.3.

$C_{16}H_{23}NO_3$ (MW = 277.37, Mass Spectroscopy (MH^+ 278))

Example B3

Synthesis of *N*-(3-methylpentanoyl)-L-alanine *iso*-butyl ester

5 Following General Procedure BB and using 3-methylpentanoic acid (Aldrich) and L-alanine *iso*-butyl ester hydrochloride (from Example BB above), the title compound was prepared as an oil. The reaction was monitored by tlc on silica gel and purification was by extraction with Et_2O followed by washes with aqueous K_2CO_3 and aqueous HCl.

10 NMR data was as follows:

1H -nmr ($CDCl_3$): δ = 6.08 (d, J = 5.9 Hz, 1H), 4.62 (quint., J = 7.3 Hz, 1H), 3.92 (m, 2H), 2.22 (m, 1H), 1.84-2.00 (m, 3H), 1.40 (d, J = 7.2 Hz, 3H), 1.35 (m, 1H), 1.20 (m, 1H), 0.85-0.96 (m, 12H).

^{13}C -nmr ($CDCl_3$): δ = 173.3, 172.1, 71.4, 47.9, 43.9, 32.3, 29.38, 29.35, 27.6, 19.10, 19.06, 18.93, 18.91, 18.72, 18.67, 11.3.

$C_{13}H_{25}NO_3$ (MW = 243.35, Mass Spectroscopy (MH^+ 244))

Example B4

Synthesis of *N*-[(4-chlorophenyl)acetyl]-L-alanine *iso*-butyl ester

20 Following General Procedure BB and using 4-chlorophenylacetic acid (Aldrich) and L-alanine *iso*-butyl ester hydrochloride (from Example BB above), the title compound was prepared as a solid having a melting point of 111°-113°C. The reaction was monitored by tlc on silica gel and purification was by extraction with Et_2O followed by washes with aqueous K_2CO_3 and aqueous HCl.

25

NMR data was as follows:

1H -nmr ($CDCl_3$): δ = 7.30 (d, J = 8.2 Hz, 2H), 7.21 (d, J = 8.3 Hz, 2H), 6.18 (d, J = 5.5 Hz, 1H), 4.57 (quint., J = 7.2 Hz, 1H), 3.88 (m, 2H), 3.53 (s, 2H), 1.91 (m, 1H), 1.36 (d, J = 7.1 Hz, 3H), 0.90 (d, J = 6.8 Hz, 6H).

30 ^{13}C -nmr ($CDCl_3$): δ = 172.8, 169.8, 133.1, 133.0, 130.6, 128.9, 71.4, 48.2, 42.6, 27.6, 18.85, 18.82, 18.4.

$C_{15}H_{20}NO_3Cl$ (MW = 297.78, Mass Spectroscopy (MH^+ 298))

Example B5

Synthesis of *N*-[(3,4-dichlorophenyl)acetyl]-L-alanine *iso*-butyl ester

5 Following General Procedure BB and using 3,4-dichlorophenylacetic acid (Aldrich) and L-alanine *iso*-butyl ester hydrochloride (from Example BB above), the title compound was prepared as a solid having a melting point of 81°-83°C. The reaction was monitored by tlc on silica gel and purification was by extraction with Et₂O followed by washes with aqueous K₂CO₃ and aqueous HCl.

10 NMR data was as follows:

¹H-nmr (CDCl₃): δ = 0.90 (d, *J* = 6.8 Hz, 6H), 1.38 (d, *J* = 7.1 Hz, 3H), 1.91 (m, 1H), 3.50 (s, 2H), 3.90 (m, 2H), 4.57 (quint., *J* = 7.1 Hz, 1H), 6.31 (d, *J* = 4.9 Hz, 1H), 7.12 (m, 1H), 7.38 (m, 2H).

15 ¹³C-nmr (CDCl₃): δ = 18.4, 18.8, 18.9, 27.6, 42.2, 48.3, 71.5, 128.6, 130.6, 131.2, 131.3, 132.6, 134.7, 169.2, 172.8.

$C_{15}H_{19}NO_3Cl_2$ (MW = 332.23, Mass Spectroscopy (MH^+ 332))

Example B6

Synthesis of *N*-[(4-methylphenyl)acetyl]-D,L-alanine *iso*-butyl ester

20 Following General Procedure BB and using 4-methylphenylacetic acid (Aldrich) and D,L-alanine *iso*-butyl ester hydrochloride (from Example BB above), the title compound was prepared as a solid having a melting point of 102°-104°C. The reaction was monitored by tlc on silica gel (*R*_f = 0.6 in 33% ethyl acetate/hexanes) and purification was by extraction with Et₂O followed by washes with aqueous K₂CO₃ and aqueous HCl.

25 NMR data was as follows:

30 ¹H-nmr (CDCl₃): δ = 0.90 (d, *J* = 6.7 Hz, 6H), 1.35 (d, *J* = 7.2 Hz, 3H), 1.91 (m, 1H), 2.34 (s, 3H), 3.55 (s, 2H), 3.88 (m, 2H), 4.58 (m, 1H), 6.05 (bd, 1H), 7.16 (s, 4H).

^{13}C -nmr (CDCl_3): $\delta = 18.5, 18.85, 18.87, 21.0, 27.6, 43.1, 48.1, 71.3, 129.2, 129.6, 131.3, 136.9, 170.6, 172.8$.

$\text{C}_{16}\text{H}_{23}\text{NO}_3$ (MW = 277.37, Mass Spectroscopy (MH^+ 278))

5

Example B7

Synthesis of *N*-[(3-pyridyl)acetyl]-D,L-alanine *iso*-butyl ester

Following General Procedure BF and using 3-pyridylacetic acid hydrochloride (Aldrich) and D,L-alanine *iso*-butyl ester hydrochloride (from Example BB above), the title compound was prepared as a solid having a melting point of 62°-64°C. The reaction was monitored by tlc on silica gel ($R_f = 0.48$ 10% methanol/dichloromethane) and purification was by silica gel chromatography.

NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 8.40$ (d, $J = 2.8$, 2H); 7.6 (m, 1H); 7.16 (m, 2H); 4.5 (quint., $J = 7.2, 7.2$, 1H); 3.8 (m, 2H); 3.48 (s, 2H); 1.8 (m, 1H); 1.30 (d, $J = 7.2$, 3H); 0.81 (d, $J = 6.7$, 6H).

^{13}C -nmr (CDCl_3): $\delta = 173.4, 170.1, 150.6, 148.8, 137.4, 131.4, 124.1, 71.9, 48.9, 40.6, 28.1, 19.5, 19.4, 18.6$.

$\text{C}_{14}\text{H}_{20}\text{N}_2\text{O}_3$ (MW = 264, Mass Spectroscopy (MH^+ 265))

20

Example B8

Synthesis of *N*-[(1-naphthyl)acetyl]-L-alanine *iso*-butyl ester

Following General Procedure BB and using 1-naphthylacetic acid (Aldrich) and L-alanine *iso*-butyl ester hydrochloride (from Example BB above), the title compound was prepared as a solid having a melting point of 69°-73°C. The reaction was monitored by tlc on silica gel and purification was by extraction with Et_2O followed by washes with aqueous K_2CO_3 and aqueous HCl.

NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 0.83$ (m, 6H), 1.25 (d, $J = 7.1$ Hz, 3H), 1.81 (m, 1H), 3.79 (m, 2H), 4.04 (2s, 2H), 4.57 (quint., $J = 7.3$ Hz, 1H), 5.99 (d, $J = 7.1$ Hz, 1H), 7.44 (m, 2H), 7.53 (m, 2H), 7.85 (m, 2H), 7.98 (m, 1H).

^{13}C -nmr (CDCl_3): $\delta = 18.2, 18.81, 18.83, 27.5, 41.5, 48.2, 71.3, 123.7, 125.6, 126.1, 126.6, 128.2, 128.5, 128.7, 130.7, 132.0, 133.9, 170.3, 172.5.$

$\text{C}_{19}\text{H}_{23}\text{NO}_3$ (MW = 313.40, Mass Spectroscopy (MH^+ 314))

5

Example B9

Synthesis of *N*-[(2-naphthyl)acetyl]-L-alanine *iso*-butyl ester

Following General Procedure BB and using 2-naphthylacetic acid (Aldrich) and L-alanine *iso*-butyl ester hydrochloride (from Example BB above), the title compound was prepared as a solid having a melting point of 128°-129°C. The reaction was monitored by tlc on silica gel and purification was by extraction with Et_2O followed by washes with aqueous K_2CO_3 and aqueous HCl.

NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 0.86$ (m, 6H), 1.35 (d, $J = 7.1$ Hz, 3H), 1.78 (m, 1H), 3.76 (s, 2H), 3.87 (m, 2H), 4.62 (quint., $J = 7.2$ Hz, 1H), 6.13 (d, $J = 7.1$ Hz, 1H), 7.41 (m, 1H), 7.48 (m, 2H), 7.74 (s, 1H), 7.83 (m, 3H).

^{13}C -nmr (CDCl_3): $\delta = 18.4, 18.82, 18.85, 27.6, 43.7, 48.2, 71.4, 125.9, 126.3, 127.2, 127.6, 127.7, 128.2, 128.7, 132.0, 132.5, 133.5, 170.3, 172.8.$

$\text{C}_{19}\text{H}_{23}\text{NO}_3$ (MW = 313.40, Mass Spectroscopy (MH^+ 314)).

20

Example B10

Synthesis of *N*-(4-phenylbutanoyl)-L-alanine *iso*-butyl ester

Following General Procedure BB and using 4-phenylbutanoic acid (Aldrich) and L-alanine *iso*-butyl ester hydrochloride (from Example BB above), the title compound was prepared as an oil. The reaction was monitored by tlc on silica gel and purification was by extraction with Et_2O followed by washes with aqueous K_2CO_3 and aqueous HCl.

NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 0.92$ (d, $J = 6.7$ Hz, 6H), 1.38 (d, $J = 7.1$ Hz, 3H), 1.96 (m, 3H), 2.21 (t, $J = 7.1$ Hz, 2H), 2.64 (t, $J = 7.3$ Hz, 2H), 3.90 (m, 2H), 4.59 (quint., $J = 7.2$ Hz, 1H), 6.31 (d, 1H), 7.16 (m, 3H), 7.24 (m, 2H).

^{13}C -nmr (CDCl_3): $\delta = 18.3, 18.75, 18.78, 26.8, 27.5, 34.9, 35.3, 47.8, 71.2, 125.7, 128.2, 128.3, 141.3, 172.1, 173.0$.

$\text{C}_{17}\text{H}_{25}\text{NO}_3$ (MW = 291.39, Mass Spectroscopy (MH^+ 292)).

5

Example B11

Synthesis of *N*-(5-phenylpentanoyl)-L-alanine *iso*-butyl ester

Following General Procedure BB and using 5-phenylpentanoic acid (Aldrich) and L-alanine *iso*-butyl ester hydrochloride (from Example BB above), the title compound was prepared as an oil. The reaction was monitored by tlc on silica gel and purification was by extraction with Et_2O followed by washes with aqueous K_2CO_3 and aqueous HCl .

10

NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 7.23$ (m, 2H), 7.17 (m, 3H), 6.30 (d, 1H), 4.59 (quint., $J = 7.3$ Hz, 1H), 3.91 (m, 2H), 2.61 (t, $J = 7.2$ Hz, 2H), 2.22 (t, $J = 7.2$ Hz, 2H), 1.93 (m, 1H), 1.66 (m, 4H), 1.38 (d, $J = 7.2$ Hz, 3H), 0.92 (d, $J = 6.7$ Hz, 6H).

15

^{13}C -nmr (CDCl_3): $\delta = 173.1, 172.3, 142.0, 128.2, 128.1, 125.6, 71.2, 47.8, 36.1, 35.5, 30.8, 27.5, 25.0, 18.80, 18.77, 18.4$.

$\text{C}_{18}\text{H}_{27}\text{NO}_3$ (MW = 305.39, Mass Spectroscopy (MH^+ 306)).

20

Example B12

Synthesis of *N*-[(4-pyridyl)acetyl]-D,L-alanine *iso*-butyl ester

Following General Procedure BF and using 4-pyridylacetic acid hydrochloride (Aldrich) and (D,L)-alanine *iso*-butyl ester hydrochloride (from Example BB above), the title compound was prepared as a solid having a melting point of $64^\circ\text{--}66^\circ\text{C}$. The reaction was monitored by tlc on silica gel ($R_f = 0.43$ 10% methanol/dichloromethane) and purification was by silica gel chromatography.

25

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 8.51 (dd, *J* = 1.6, 2.8, 1.6, 2H); 7.23 (dd, *J* = 4.3, 1.6, 4.4, 2H); 6.71 (d, *J* = 6.8, 1H); 4.56 (quint., *J* = 7.3, 7.2, 1H); 3.88 (m, 2H); 3.53 (s, 2H); 1.89 (m, 1H); 1.36 (d, *J* = 7.2, 3H); 0.88 (d, *J* = 6.7, 6H).

¹³C-nmr (CDCl₃): δ = 173.5, 169.3, 150.5, 144.4, 125.1, 72.1, 48.9, 43.0,
5 28.2, 19.5, 19.5, 18.9.

C₁₄H₂₀N₂O₃ (MW = 264, Mass Spectroscopy (MH⁺ 265))

Example B13

Synthesis of N-(phenylacetyl)-L-alanine *iso*-butyl ester

10 Following General Procedure BB and using phenylacetyl chloride (Aldrich) and L-alanine *iso*-butyl ester hydrochloride (from Example BB above), the title compound was prepared as a solid having a melting point of 45°-47°C. The reaction was monitored by tlc on silica gel and purification was by extraction with Et₂O followed by washes with aqueous K₂CO₃ and aqueous HCl.

15 NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.24-7.39 (m, 5H), 6.14 (d, 1H), 4.58 (t, *J* = 7.3 Hz, 1H), 3.88 (m, 2H), 3.58 (s, 2H), 1.90 (m, 1H), 1.35 (d, *J* = 7.2 Hz, 3H), 0.89 (d, *J* = 6.7 Hz, 6H).

¹³C-nmr (CDCl₃): δ = 172.8, 170.4, 134.5, 129.3, 128.9, 127.2, 71.3, 48.1,
20 43.5, 27.5, 18.9, 18.8, 18.4.

C₁₅H₂₁NO₃ (MW = 263.34, Mass Spectroscopy (MH⁺ 264)).

Example B14

Synthesis of 2-[(3,4-dichlorophenyl)acetamido]butyric acid *iso*-butyl ester

25 Following General Procedure BI above and using 3,4-dichlorophenylacetic acid (Aldrich) and *iso*-butyl 2-aminobutyrate (prepared following General Procedure BJ above) the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

30 NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.36 (m, 3H), 6.03 (bd, 1H), 4.54 (m, 1H), 3.87 (m, 2H), 3.49 (s, 2H), 1.93 (m, 2H), 1.72 (m, 1H), 0.88 (d, 6H), 0.80 (t, 3H).

Example B15

5 **Synthesis of 2-[(3-methoxyphenyl)acetamido]butyric acid *iso*-butyl ester**

Following General Procedure BI above and using 3-methoxyphenylacetic acid (Aldrich) and *iso*-butyl 2-aminobutyrate (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 6.75 (m, 4H), 5.93 (bd, 1H), 4.51 (m, 1H), 3.83 (m, 2H), 3.75 (s, 2H), 3.52 (s, 2H), 1.82 (m, 2H), 1.60 (m, 1H), 0.84 (d, 6H), 0.74 (t, 3H).

15 C₁₇H₂₅NO₄ (MW = 307.39, Mass Spectroscopy (MH⁺ 309)).

Example B16

Synthesis of 2-[(4-nitrophenyl)acetamido]butyric acid *iso*-butyl ester

20 Following General Procedure BI above and using 4-nitrophenylacetic acid (Aldrich) and *iso*-butyl 2-aminobutyrate (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

25 ¹H-nmr (CDCl₃): δ = 8.16 (d, 2H), 7.44 (d, 2H), 6.04 (bd, 1H), 4.55 (m, 1H), 3.86 (m, 2H), 3.66 (s, 2H), 1.86 (m, 2H), 1.67 (m, 1H), 0.85 (d, 6H), 0.81 (t, 3H).

C₁₆H₂₂N₂O₅ (MW = 322.36, Mass Spectroscopy (MH⁺ 323)).

30

Example B17

Synthesis of 2-[(3,4-methylenedioxyphenyl)acetamido]butyric acid *iso*-butyl ester

Following General Procedure BI above and using 3,4-(methylenedioxy)-phenyl acetic acid (Aldrich) and *iso*-butyl 2-aminobutyrate (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 6.72 (m, 3H), 5.92 (bd, 1H), 4.54 (m, 1H), 3.86 (m, 2H), 3.66 (s, 2H), 1.86 (m, 2H), 1.66 (m, 1H), 0.89 (d, 6H), 0.79 (t, 3H).

Example B18

Synthesis of 2-[(thien-3-yl)acetamido]butyric acid *iso*-butyl ester

Following General Procedure BI above and using 3-thiopheneacetic acid (Aldrich) and *iso*-butyl 2-aminobutyrate (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.37 (m, 1H), 7.16 (m, 1H), 7.04 (m, 1H), 6.05 (bd, 1H), 4.57 (m, 1H), 3.66 (s, 2H), 1.93 (m, 2H), 1.67 (m, 1H), 0.91 (d, 6H), 0.86 (t, 3H).

Example B19

Synthesis of 2-[(4-chlorophenyl)acetamido]butyric acid *iso*-butyl ester

Following General Procedure BI above and using 4-chlorophenylacetic acid (Aldrich) and *iso*-butyl 2-aminobutyrate (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.22 (m, 2H), 7.11 (m, 2H), 5.80 (m, 1H), 4.44 (m, 1H), 3.78 (m, 2H), 3.43 (s, 2H), 1.77 (m, 2H), 1.56 (m, 1H), 0.83 (d, 6H) 0.71 (t, 3H).

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Example B20

Synthesis of 2-[(3-nitrophenyl)acetamido]butyric acid *iso*-butyl ester

Following General Procedure BI above and using 3-nitrophenylacetic acid (Aldrich) and *iso*-butyl 2-aminobutyrate (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

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NMR data was as follows:

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¹H-nmr (CDCl₃): δ = 8.15 (m, 2H), 7.65 (m, 1H), 6.08 (m, 1H), 4.46 (m, 1H), 3.92 (m, 2H), 3.68 (s, 2H), 1.91 (m, 2H), 1.75 (m, 1H), 0.98 (d, 6H) 0.71 (t, 3H).

Example B21

Synthesis of 2-[(2-hydroxyphenyl)acetamido]butyric acid *iso*-butyl ester

Following General Procedure BI above and using 2-hydroxyphenylacetic acid (Aldrich) and *iso*-butyl 2-aminobutyrate (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

20

NMR data was as follows:

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¹H-nmr (CDCl₃): δ = 7.14 (m, 1H), 7.01 (m, 1H), 6.93 (m, 1H), 6.79 (m, 1H), 6.46 (m, 1H), 4.51 (m, 1H), 3.87 (m, 2H), 3.57 (s, 2H), 2.01 (m, 2H), 1.75 (m, 1H), 0.89 (d, 6H), 0.85 (t, 3H).

Example B22

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Synthesis of 2-[(2-naphthyl)acetamido]butyric acid *iso*-butyl ester

Following General Procedure BI above and using 2-naphthylacetic acid (Aldrich) and *iso*-butyl 2-aminobutyrate (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.83 (m, 7H), 5.95 (m, 1H), 4.58 (m, 1H), 3.84 (m, 2H), 3.75 (s, 2H), 1.89 (m, 2H), 1.63 (m, 1H), 0.91 (d, 6H), 0.81 (t, 3H).

C₂₀H₂₅NO₃ (MW = 327.42, Mass Spectroscopy (MH⁺ 328)).

Example B23

Synthesis of 2-[(2,4-dichlorophenyl)acetamido]butyric acid *iso*-butyl ester

Following General Procedure BI above and using 2,4-dichlorophenylacetic acid (Aldrich) and *iso*-butyl 2-aminobutyrate (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.49 (m, 1H), 7.22 (m, 2H), 5.98 (m, 1H), 4.52 (m, 1H), 3.86 (m, 2H), 3.61 (s, 2H), 1.84 (m, 2H), 1.62 (m, 1H), 0.87 (d, 6H), 0.80 (t, 3H).

Example B24

Synthesis of 2-[(4-bromophenyl)acetamido]butyric acid *iso*-butyl ester

Following General Procedure BI above and using 4-bromophenylacetic acid (Aldrich) and *iso*-butyl 2-aminobutyrate (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.43 (d, 2H), 7.19 (d, 2H) 5.85 (m, 1H), 4.51 (m, 1H), 3.81 (m, 2H), 3.47 (s, 2H), 1.84 (m, 2H), 1.61 (m, 1H) 0.84 (d, 6H), 0.76 (t, 3H).

C₁₆H₂₂NO₃Br (MW = 356.26, Mass Spectroscopy (MH⁺ 358)).

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Example B25

Synthesis of 2-[(3-chlorophenyl)acetamido]butyric acid *iso*-butyl ester

Following General Procedure BI above and using 3-chlorophenylacetic acid (Aldrich) and *iso*-butyl 2-aminobutyrate (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.25 (m, 3H), 7.12 (m, 1H) 5.80 (m, 1H), 4.52 (m, 1H), 3.86 (m, 2H), 3.50 (s, 2H), 1.87 (m, 2H), 1.67 (m, 1H) 0.88 (d, 6H), 0.77 (t, 3H).

C₁₆H₂₂NO₃Cl (MW = 311.81 Mass Spectroscopy (MH⁺ 313)).

Example B26

Synthesis of 2-[(3-fluorophenyl)acetamido]butyric acid *iso*-butyl ester

Following General Procedure BI above and using 3-fluorophenylacetic acid (Aldrich) and *iso*-butyl 2-aminobutyrate (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.31 (m, 1H), 7.01 (m, 3H) 5.95 (m, 1H), 4.54 (m, 1H), 3.84 (m, 2H), 3.54 (s, 2H), 1.88 (m, 2H), 1.65 (m, 1H) 0.87 (d, 6H), 0.81 (t, 3H).

C₁₆H₂₂NO₃F (MW = 295.35 Mass Spectroscopy (MH⁺ 296)).

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Example B27

Synthesis of 2-[(benzothiazol-4-yl)acetamido]butyric acid *iso*-butyl ester

Following General Procedure BI above and using 4-benzothiazol-4-yl acetic acid (Chemservice) and *iso*-butyl 2-aminobutyrate (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.82 (m, 1H), 7.51-7.21 (m, 4H) 5.84 (m, 1H), 4.51 (m, 1H), 3.90 (s, 2H), 3.79 (m, 2H), 1.78 (m, 2H), 1.58 (m, 1H) 0.80 (d, 6H), 0.66 (t, 3H).

Example B28

Synthesis of 2-[(2-methylphenyl)acetamido]butyric acid *iso*-butyl ester

Following General Procedure BI above and using 2-methylphenylacetic acid (Aldrich) and *iso*-butyl 2-aminobutyrate (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.18 (m, 4H), 5.79 (m, 1H), 4.54 (m, 1H), 3.85 (m, 2H), 3.59 (s, 2H), 3.29 (s, 3H), 1.81 (m, 2H), 1.59 (m, 1H) 0.87 (d, 6H), 0.77 (t, 3H).

C₁₇H₂₅NO₃ (MW = 291.39 Mass Spectroscopy (M⁺ 291)).

Example B29

Synthesis of 2-[(2-fluorophenyl)acetamido]butyric acid *iso*-butyl ester

Following General Procedure BI above and using 2-fluorophenylacetic acid (Aldrich) and *iso*-butyl 2-aminobutyrate (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc

on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.28 (m, 1H), 7.09 (m, 3H) 6.03 (m, 1H), 4.54 (m, 1H), 3.87 (m, 2H), 3.57 (s, 2H), 1.89 (m, 2H), 1.64 (m, 1H) 0.88 (d, 6H), 0.80 (t, 3H).

Example B30

Synthesis of 2-[(4-fluorophenyl)acetamido]butyric acid *iso*-butyl ester

Following General Procedure BI above and using 4-fluorophenylacetic acid (Aldrich) and *iso*-butyl 2-aminobutyrate (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.20 (m, 2H), 6.97 (m, 2H) 5.87 (m, 1H), 4.492 (m, 1H), 3.83 (m, 2H), 3.48 (s, 2H), 1.86 (m, 2H), 1.60 (m, 1H) 0.87 (d, 6H), 0.78 (t, 3H).

C₁₆H₂₂NO₃F (MW = 295.35 Mass Spectroscopy (MH⁺ 296)).

Example B31

Synthesis of 2-[(3-bromophenyl)acetamido]butyric acid *iso*-butyl ester

Following General Procedure BI above and using 3-bromophenylacetic acid (Aldrich) and *iso*-butyl 2-aminobutyrate (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.45 (m, 2H), 7.23 (m, 2H) 5.95 (m, 1H), 4.55 (m, 1H) 3.84 (m, 2H) 3.55 (s, 2H), 1.89 (m, 2H), 1.68 (m, 1H) 0.91 (d, 6H), 0.81 (t, 3H).

$C_{16}H_{22}NO_3Br$ (MW = 356.26 Mass Spectroscopy (M^+ 357)).

Example B32

**Synthesis of 2-[(3-trifluoromethylphenyl)acetamido]butyric acid
iso-butyl ester**

Following General Procedure BI above and using 3-trifluoromethyl-phenylacetic acid (Aldrich) and *iso*-butyl 2-aminobutyrate (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

1H -nmr ($CDCl_3$): δ = 7.52 (m, 1H), 7.47 (m, 2H) 6.01 (m, 1H), 4.56 (m, 1H), 3.86 (m, 2H), 3.61 (s, 2H), 1.84 (m, 2H), 1.62 (m, 1H) 0.87 (d, 6H), 0.80 (t, 3H).

$C_{17}H_{22}NO_3F_3$ (MW = 345.36 Mass Spectroscopy (MH^+ 345)).

Example B33

Synthesis of 2-[(2-thienyl)acetamido]butyric acid *iso*-butyl ester

Following General Procedure BI above and using 2-thiopheneacetic acid (Aldrich) and *iso*-butyl 2-aminobutyrate (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

1H -nmr ($CDCl_3$): δ = 6.89 (m, 3H), 6.07 (bd, 1H), 4.50 (m, 1H), 3.82 (m, 2H), 3.71 (s, 2H), 1.85 (m, 2H), 1.62 (m, 1H), 0.81 (d, 6H), 0.75 (t, 3H).

$C_{14}H_{21}NO_3S$ (MW = 283.39, Mass Spectroscopy (MH^+ 284)).

Example B34

Synthesis of 2-(phenylacetamido)butyric acid *iso*-butyl ester

Following General Procedure BH above and using phenylacetic acid (Aldrich) and *iso*-butyl 2-aminobutyrate (prepared following General Procedure

BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by chromatography on silica gel using 9:1 toluene:EtOAc as the eluant.

NMR data was as follows:

5 ^1H -nmr (CDCl_3): δ = 7.17-7.28 (m, 5H), 6.23 (bd, 1H), 4.51 (m, 1H), 3.86 (m, 2H), 3.54 (s, 2H), 1.87 (m, 2H), 1.62 (m, 1H), 0.87 (d, 6H), 0.78 (t, 3H).
 $\text{C}_{16}\text{H}_{23}\text{NO}_3$ (MW = 277.36, Mass Spectroscopy (MH^+ 277)).

Example B35

10 **Synthesis of *N*-(phenylacetyl)valine 2-methylbutyl ester**

Step A. Preparation of *N*-(phenylacetyl) valine

To a stirred solution of 5.15 g (44 mmol) of valine (Bachem) in 50 mL (100 mmol) of 2N NaOH cooled to 0°C was added dropwise 5.3 mL (40 mmol) of phenylacetyl chloride (Aldrich). A colorless oil precipitated. The reaction
15 mixture was allowed to warm to room temperature and stirred for 18 hours, washed with 50 mL diethyl ether, acidified to pH 2-3 with aqueous HCl. The white precipitate formed was filtered off, washed thoroughly with water, followed by diethyl ether to give 7.1 g (30 mmol, 69% yield) of the title compound.

20 NMR data was as follows:

^1H -nmr ($\text{DMSO}-d_6$): δ = 12.63 (s, 1H), 8.25 (d, J = 8.6 Hz, 1H), 7.27 (m, 5H), 4.15 (m, 1H), 3.56 (d, J = 13.8 Hz, 1H), 3.47 (d, J = 13.8 Hz, 1H), 2.05 (m, 1H), 0.87 (d, J = 6.8, Hz, 3H), 0.84 (d, J = 6.8 Hz, 3)

25 ^{13}C -nmr ($\text{DMSO}-d_6$): δ = 173.2, 170.4, 136.6, 129.0, 128.2, 126.3, 57.1, 41.9, 30.0, 19.2, 18.0

$\text{C}_{13}\text{H}_{17}\text{NO}_3$ (MW=235.29; Mass Spectroscopy (MH^+ = 236))

Step B. Synthesis of *N*-(phenylacetyl)valine 2-methylbutyl ester

30 Following General Procedure BC and using the *N*-(phenylacetyl) valine prepared in Step A above and 2-methylbutan-1-ol (Aldrich), the title compound

was prepared as a diastereomeric mixture. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.25-7.40 (m, 5H), 5.95 (d, 1H), 4.56 (m, 1H), 3.84-4.00 (m, 2H), 3.61 (s, 2H), 2.10 (m, 1H), 1.68 (m, 1H), 1.38 (m, 1H), 1.15 (m, 1H), 0.82-0.94 (m, 9H), 0.76 (d, 3H).

¹³C-nmr (CDCl₃): δ = 171.84, 171.81, 170.7, 134.6, 129.31, 129.27, 128.9, 127.3, 69.8, 57.0, 43.7, 33.9, 31.3, 25.9, 25.8, 18.9, 17.4, 16.34, 16.27, 11.12, 11.07.

C₁₈H₂₇NO₃ (MW = 305.42, Mass Spectroscopy (MH 306)).

Example B36

Synthesis of *N*-(phenylacetyl)-*L*-methionine *iso*-butyl ester

L-Methionine (0.129g, 0.869 mmols) (Aldrich) was taken-up in dioxane (5.0 mL) and treated with a saturated solution of sodium bicarbonate (5.0 mL) followed by phenylacetyl chloride (Aldrich) (0.114 mL, 0.822 mmols). After stirring for 17 hours at room temperature the mixture was diluted with ethyl acetate, the layers separated and the aqueous layer acidified to pH 2 with 5N HCl. The crude product was extracted into ethyl acetate, dried over sodium sulfate, vacuum dried and used without further purification.

N-phenylacetyl-*L*-methionine (0.1285 g, 0.447 mmol) was dissolved in 3.0 mL dioxane and *iso*-butyl alcohol (0.2 mL) and treated with EDC (0.094 g, 0.492 mmol), and catalytic DMAP (0.015g). After stirring for 17 hours at 23°C, the mixture was evaporated at reduced pressure to an oil, the residue was diluted in EtOAc and washed with 0.1 N HCl and saturated sodium bicarbonate. Chromatography on silica gel using 98:2 CHCl₃/MeOH as eluant provided the pure product.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.4-7.23 (m, 5H), 6.14 (bd, 1H), 4.70 (m, 1H), 3.89 (d, 2H), 3.62 (s, 2H), 2.43 (m, 2H), 2.12 (m, 1H), 1.93 (m, 2H), 0.94 (d, 6H).

C₁₇H₂₅NO₃S (MW = 323.17, Mass Spectroscopy (M⁺ 323))

Example B37

Synthesis of *N*-(phenylacetyl)-L-leucine *iso*-butyl ester

L-Leucine (Aldrich) (0.114g, 0.869 mmols) was taken-up in dioxane (5.0 mL) and treated with a saturated solution of sodium bicarbonate (5.0 mL) followed by phenylacetyl chloride (Aldrich) (0.114 mL, 0.822 mmols). After stirring for 17 hours at room temperature the mixture was diluted with ethyl acetate, the layers separated and the aqueous layer acidified to pH 2 with 5N HCl. The crude product was extracted into ethyl acetate, dried over sodium sulfate, vacuum dried and used without further purification.

N-Phenylacetyl-L-leucine (0.0081 g, 0.038 mmol) was dissolved in 2.0 mL CHCl₃ (EtOH free) and *iso*-butyl alcohol (0.055 mL) and treated with P-EPC (100 mg, 0.87 milliequivalents). The mixture was rotated for 4 days, filtered through a plug of cotton and the filtrate evaporated at reduced pressure to an oil which was sufficiently pure for testing.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.22 (m, 5H), 5.57 (d, 1H), 4.35 (m, 1H), 3.35 (m, 3H), 1.35 (m, 4H), 0.68 (m, 9H).

C₁₈H₂₇NO₃ (MW = 305.40, Mass Spectroscopy (M⁺ 305)).

Example B38

Synthesis of *N*-[(3-chlorophenyl)acetyl]alanine 3-methylbut-2-enyl ester

Following General Procedure BC above and using N-(3-chlorophenylacetyl) alanine (from Example BD above) and 3-methylbut-2-en-1-ol (Aldrich), the title compound can be prepared. The reaction was monitored by tlc on silica gel and purification was by liquid chromatography using 30% EtOAc/hexane as the eluant.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.39-7.16 (m, 4H), 6.06 (bd, 1H), 5.38-5.29 (m, 1H), 4.63 (d, *J* = 9Hz, 2H), 3.56 (s, 2H), 1.79 (s, 3H), 1.7 (s, 3H), 1.39 (d, *J* = 9Hz, 3H).

Example B39

Synthesis of *N*-[(3-chlorophenyl)acetyl]alanine cyclopropylmethyl ester

Following General Procedure BC above, and using *N*-(3-chlorophenylacetyl)alanine (from Example BD above) and cyclopropylmethanol (Aldrich), the title compound can be prepared. The reaction was monitored by tlc on silica gel and purification was by liquid chromatography using 3:7 EtOAc:hexane as the eluant.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.2-7.1 (m, 4H), 6.09 (bs, 1H), 4.6 (dq, *J* = 9 Hz, 1H), 3.96 (dd, *J* = 9Hz, 2H), 3.59 (s, 2H), 1.2 (d, *J* = 9Hz, 3H), 1.2-1.0 (m, 1H), 0.603-0.503 (m, 2H), 0.300-0.203 (m, 2H).

Example B40

Synthesis of *N*-[(3-chlorophenyl)acetyl]alanine 2-thienylmethyl ester

Following General Procedure BC above, and using *N*-(3-chlorophenylacetyl)alanine (from Example BD above) and 2-thiophenemethanol (Aldrich) the title compound can be prepared. The reaction was monitored by tlc on silica gel and purification was by liquid chromatography using 3:7 EtOAc:hexane as the eluant.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.37-6.97 (m, 7H), 5.97 (q, *J* = 14 Hz, 2H), 4.6 (dq, *J* = 9 Hz, 1H), 3.76 (s, 2H), 1.38 (d, *J* = 9Hz, 3H).

Example B41

Synthesis of *N*-[(3-chlorophenyl)acetyl]alanine (1-methylcyclopropyl)methyl ester

Following General Procedure BC above, and using *N*-(3-chlorophenylacetyl)alanine (from Example BD above) and (1-methylcyclopropyl)methanol (Aldrich) the title compound can be prepared. The reaction was monitored by tlc on silica gel and purification was by liquid chromatography using 3:7 EtOAc:hexane as the eluant.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 8.6 (bd, *J* = 9 Hz, 1H), 3.86 (q, *J* = 14 Hz, 2H), 3.4 (s, 2H), 2.29 (q, *J* = 9 Hz, 1H), 1.3 (d, *J* = 9 Hz, 3H), 1.03 (s, 3H), 0.5-0.4 (m, 2H), 0.4-0.28 (m, 2H).

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Example B42

Synthesis of *N*-[(3-chlorophenyl)acetyl]alanine 3-thienylmethyl ester

Following General Procedure BC above, and using *N*-(3-chlorophenylacetyl)alanine (from Example BD above) and 3-thiophenemethanol (Aldrich) the title compound can be prepared. The reaction was monitored by tlc on silica gel and purification was by liquid chromatography using 3:7 EtOAc:hexane as the eluant.

10

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 8.03 (bd, *J* = 9 Hz, 1H), 7.56-7.5 (m, 1H), 7.47 (bs, 1H), 7.4-7.17 (m, 4H), 7.06 (d, *J* = 9 Hz, 1H), 5.1 (s, 2H), 4.3 (dq, 1H), 1.3 (d, *J* = 9 Hz, 3H).

15

Example B43

Synthesis of *N*-[(3-chlorophenyl)acetyl]alanine 2-methylcyclopentyl ester

Following General Procedure BC above, and using *N*-(3-chlorophenylacetyl)alanine (from Example BD above) and 2-methylcyclopentanol (Aldrich) the title compound can be prepared. The reaction was monitored by tlc on silica gel and purification was by liquid chromatography using 3:7 EtOAc:hexane as the eluant.

20

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.39-7.16 (m, 4H), 6.3 (bd, 1H), 4.79-4.7 (m, 1H), 4.6-4.25 (m, *J* = 9 Hz, 1H), 3.577 (s, 2H), 2.09-1.8 (m, 2H), 1.74-1.6 (m, 2H), 1.39 (dd, *J* = 9 Hz, 3H), 1.2 (dt, *J* = 9 Hz, 1H), 0.979 (dd, *J* = 9 Hz, 2H)

25

C₁₇H₂₂NO₃Cl (MW = 323.82, Mass Spectroscopy (MH⁺ 323).

30

Example B44

Synthesis of *N*-[(3-chlorophenyl)acetyl]alanine 2-methylprop-2-enyl ester

Following General Procedure BC above, and using N-(3-chlorophenylacetyl alanine (from Example BD above) and 2-methylprop-2-en-1-ol (Aldrich) the title compound can be prepared. The reaction was monitored by tlc on silica gel and purification was by liquid chromatography using 3:7 EtOAc:hexane as the eluant.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.39-7.16 (m, 4H), 6.03 (bs, 1H), 4.77 (s, 2H), 4.7-4.29 (m, 3H), 2.59 (s, 2H), 1.73 (s, 3H), 1.43 (d, *J* = 9 Hz, 3H)

C₁₅H₁₈NO₃Cl (MW = 295.76, Mass Spectroscopy (MH⁺ 295)).

Example B45

Synthesis of *N*-[(3-chlorophenyl)acetyl]alanine cyclohex-2-enyl ester

Following General Procedure BC above, and using N-(3-chlorophenylacetyl alanine (from Example BD above) and cyclohex-2-en-1-ol (Aldrich) the title compound can be prepared. The reaction was monitored by tlc on silica gel and purification was by liquid chromatography using 3:7 EtOAc:hexane as the eluant.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 8.6 (bd, *J* = 9 Hz, 1H), 7.4-7.2 (m, 4H), 6.0-5.8 (m, 1H), 5.7-5.5 (m, 1H), 5.1 (bs, 1H), 4.13-4.29 (m, 1H), 3.5 (s, 2H), 2.1-1.9 (m, 2H), 1.8-1.69 (m, 1H), 1.69-1.49 (m, 4H), 1.3 (dd, *J* = 9 Hz, 3H)

C₁₇H₂₀NO₃Cl (MW = 321.8, Mass Spectroscopy (MH⁺ 321.2)).

Example B46

Synthesis of *N*-[(2-phenylbenzoxazol-5-yl)acetyl]alanine *iso*-butyl ester

Following General Procedure BI above, and using 5-(2-phenylbenzoxazol)-yl-acetic acid (CAS# 62143-69-5) and alanine *iso*-butyl ester (prepared following General Procedure BJ above), the title compound was prepared.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 8.24 (m, 3H), 7.68 (m, 1H), 7.51 (m, 5H), 6.04 (m, 1H), 4.58 (m, 1H), 3.85 (m, 2H), 3.68 (s, 2H), 1.9 (m, 1H), 1.35 (d, 3H), 0.87 (d, 6H).

C₂₂H₂₄N₂O₄ (MW = 380, Mass Spectroscopy (MH⁺ 381)).

5

Example B47

Synthesis of *N*-[(3-methylthiophenyl)acetyl]alanine *iso*-butyl ester

Following General Procedure BI above, and using 3-methylthiophenylacetic acid (CAS# 18698-73-2) and alanine *iso*-butyl ester (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.14 (m, 2H), 7.01 (m, 1H), 4.56 (m, 1H), 3.88 (m, 2H), 3.54 (s, 2H), 2.46 (s, 3H), 1.89 (m, 1H), 1.35 (d, 3H) 0.85 (d, 6H).

C₁₆H₂₃NO₃S (MW = 309, Mass Spectroscopy (MH⁺ 310)).

Example B48

Synthesis of *N*-4-[(2-furyl)acetyl]alanine *iso*-butyl ester

Following General Procedure BI above, and using 2-furylacetic acid (CAS# 2745-26-8) and alanine *iso*-butyl ester (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.36 (m, 1H), 6.34 (m, 1H), 6.21 (m, 1H), 4.56 (m, 1H), 3.91 (m, 2H), 3.61 (s, 2H), 1.92 (m, 1H), 1.38 (d, 3H) 0.89 (d, 6H).

C₁₃H₁₉NO₄ (MW = 253, Mass Spectroscopy (MH⁺ 254)).

30

Example B49

Synthesis of *N*-[(benzofuran-2-yl)acetyl]alanine *iso*-butyl ester

Following General Procedure BI above, and using benzofuran-2-ylacetic acid (Maybridge) and alanine *iso*-butyl ester (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.51 (m, 1H), 7.44 (m, 1H), 7.25 (m, 2H), 6.67 (s, 1H), 4.60 (m, 1H), 3.87 (m, 2H), 3.77 (s, 2H), 1.88 (m, 1H), 1.38 (d, 3H), 0.87 (d, 6H).

C₁₇H₂₁NO₄ (MW = 303, Mass Spectroscopy (MH⁺ 304)).

Example B50

Synthesis of *N*-[(benzothiophen-3-yl)acetyl]alanine *iso*-butyl ester

Following General Procedure BI above, and using thianaphthen-3-ylacetic acid (Lancaster) and alanine *iso*-butyl ester (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.89 (m, 1H), 7.76 (m, 1H), 7.38 (m, 3H), 6.07 (m, 1H), 4.57 (m, 1H), 3.92 (m, 2H), 3.82 (s, 4H), 1.84 (m, 1H), 1.32 (d, 3H) 0.85 (d, 6H).

C₁₇H₂₁NO₃S (MW = 319, Mass Spectroscopy (MH⁺ 320)).

Example B51

Synthesis of *N*-[(2-chloro-5-thienyl)acetyl]alanine *iso*-butyl ester

Following General Procedure BI above, and using 5-chloro-2-thienyl)acetic acid (CAS# 13669-19-7) and alanine *iso*-butyl ester (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 6.77 (m, 1H), 6.68 (d, 1H), 6.31 (bm, 1H), 4.59 (m, 1H), 3.91 (m, 2H), 3.38 (s, 2H), 1.90 (m, 1H), 1.39 (d, 3H) 0.89 (d, 6H).

C₁₃H₁₈NO₃SCl (MW = 303, Mass Spectroscopy (MH⁺ 303)).

5

Example B52

Synthesis of *N*-[(3-methylisoxazol-5-yl)acetyl]alanine *iso*-butyl ester

Following General Procedure BI above, and using (3-methyl-isoxazol-5-yl)acetic acid (CAS# 19668-85-0) and alanine *iso*-butyl ester (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 6.07 (s, 2H), 4.56 (m, 1H), 3.92 (m, 2H), 3.68 (s, 2H), 2.29 (s, 3H), 1.94 (m, 1H), 1.89 (d, 3H) 0.91 (d, 6H).

C₁₃H₂₀N₂O₄ (MW = 268, Mass Spectroscopy (MH⁺ 269)).

Example B53

Synthesis of *N*-[(2-phenylthiothienyl)acetyl]alanine *iso*-butyl ester

Following General Procedure BI above, and using (2-phenyl-thiothienyl)acetic acid and alanine *iso*-butyl ester (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.21-7.11 (m, 6H), 6.92 (d, 1H), 4.56(m, 1H), 3.87 (m, 2H), 3.72 (s, 2H), 1.94 (m, 1H), 1.38 (d, 3H) 0.89 (d, 6H).

C₁₉H₂₃NO₃S₂ (MW = 377, Mass Spectroscopy (MH⁺ 378)).

30

Example B54

Synthesis of *N*-[(6-methoxybenzothiophen-2-yl)acetyl]alanine *iso*-butyl ester

Following General Procedure BI above, and using (6-methoxythianaphthen-2-yl)acetic acid and alanine *iso*-butyl ester (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.59 (d, 1H), 7.33 (d, 1H), 7.16 (s, 1H), 7.03 (dd, 1H), 4.56 (m, 1H), 3.87(s, 3H), 3.84 (m, 2H), 3.76 (s, 2H), 1.85 (m, 1H), 1.30 (d, 3H) 0.86 (d, 6H).

C₁₈H₂₃NO₄S (MW = 349, Mass Spectroscopy (MH⁺ 350)).

Example B55

Synthesis of *N*-[(3-phenyl-1,2,4-thiadiazol-5-yl)acetyl]alanine *iso*-butyl ester

Following General Procedure BI above, and using (3-phenyl-1,2,4-thiadiazol-5-yl)acetic acid (CAS# 90771-06-5) and alanine *iso*-butyl ester (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.47 (m, 5H), 4.66 (m, 1H), 4.16 (s, 2H), 3.91 (m, 2H), 1.93 (m, 1H), 1.48 (d, 3H) 0.93 (d, 6H).

C₁₇H₂₁N₃O₃S (MW = 347, Mass Spectroscopy (MH⁺ 348)).

Example B56

Synthesis of *N*-[2-phenyloxazol-4-yl]acetyl]alanine *iso*-butyl ester

Following General Procedure BI above, and using (2-phenyloxazol-4-yl)acetic acid (CAS# 22086-89-1) and alanine *iso*-butyl ester (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

Example B57

Synthesis of N-[(3-methylphenyl)acetyl]alanine *iso*-butyl ester

Following General Procedure BI above, and using 3-methylphenylacetic acid (Aldrich) and alanine *iso*-butyl ester (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.21 (m, 1H), 7.07 (m, 3H), 4.54 (m, 1H), 3.83 (m, 2H), 3.52 (s, 2H), 2.35 (s, 3H), 1.87 (m, 1H), 1.32 (d, 3H), 0.88 (d, 6H).

C₁₆H₂₃NO₃ (MW = 277, Mass Spectroscopy (MH⁺ 278)).

Example B58

Synthesis of N-[(2,5-difluorophenyl)acetyl]alanine *iso*-butyl ester

Following General Procedure BI above, and using 2,5-difluorophenylacetic acid (Aldrich) and alanine *iso*-butyl ester (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.08-6.94 (m, 3H), 4.57 (m, 1H), 3.91 (m, 2H), 3.56 (s, 2H), 1.92 (m, 1H), 1.41 (d, 3H), 0.91 (d, 6H).

C₁₅H₁₉NO₃F₂ (MW = 299, Mass Spectroscopy (MH⁺ 300)).

25

Example B59

Synthesis of N-[(3,5-difluorophenyl)acetyl]alanine *iso*-butyl ester

Following General Procedure BI above, and using 3,5-difluorophenylacetic acid (Aldrich) and alanine *iso*-butyl ester (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 6.81 (m, 2H), 6.74 (m, 1H), 6.06 (m, 1H), 4.57 (m, 1H), 3.92 (m, 2H), 3.51 (s, 2H), 1.94 (m, 1H), 1.36 (d, 3H) 0.87 (d, 6H).

C₁₅H₁₉NO₃F₂ (MW = 299, Mass Spectroscopy (MH⁺ 300)).

5

Example B60

Synthesis of *N*-[(3-thienyl)acetyl]alanine *iso*-butyl ester

Following General Procedure BI above, and using 3-thiopheneacetic acid (Aldrich) and alanine *iso*-butyl ester (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

10

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.33 (m, 1H), 7.14 (m, 1H), 7.01 (m, 1H), 6.09 (m, 1H), 4.58 (m, 1H), 3.88 (m, 2H), 3.60 (s, 2H), 1.91 (m, 1H), 1.37 (d, 3H) 0.92 (d, 6H).

15

Optical Rotation: [α]_D²⁵ -52 (c 1 MeOH) @ 589 nm.

C₁₃H₁₉NO₃S (MW = 269, Mass Spectroscopy (MH⁺ 269)).

20

Example B61

Synthesis of *N*-[(4-methylphenyl)acetyl]-L-alanine *iso*-butyl ester

Following General Procedure BI above, and using 4-methylphenylacetic acid (Aldrich) and L-alanine *iso*-butyl ester (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by filtration as described in the general procedure.

25

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.11 (s, 4H), 5.93 (m, 1H), 4.58 (m, 1H), 3.88 (m, 2H), 3.54 (s, 2H), 2.33 (s, 3H), 1.89 (m, 1H), 1.32 (d, 3H), 0.89 (d, 6H).

30

C₁₆H₂₃NO₃ (MW = 277.35, Mass Spectroscopy (MH⁺ 278)).

Example B62

**Synthesis of *N*-(phenylacetyl)-L-alanine S-1-(methoxycarbonyl)
iso-butyl ester**

Following General Procedure BK and using (S)-(+)-2-hydroxy-2-methylbutyric acid (Aldrich) in place of the amino acid, methyl (S)-(+)-2-hydroxy-2-methylbutyrate was prepared.

Methyl (S)-(+)-2-hydroxy-2-methylbutyrate was then coupled with carbobenzyloxy-L-alanine (Aldrich) using General Procedure BE to provide carbobenzyloxy-L-alanine S-1-(methoxycarbonyl) *iso*-butyl ester.

Carbobenzyloxy-L-alanine S-1-(methoxycarbonyl) *iso*-butyl ester (1.0 g) was then dissolved in 20 mL of methanol and 6N HCl (0.5 mL) and 10% palladium on carbon (0.1 g) were added. This reaction mixture was hydrogenated at 40 psi of hydrogen on a Parr apparatus for 5 hours at room temperature and then filtered through a pad of Celite. The filtrate was concentrated at reduced pressure to provide L-alanine S-1-(methoxycarbonyl) *iso*-butyl ester hydrochloride (98% yield).

L-Alanine S-1-(methoxycarbonyl) *iso*-butyl ester hydrochloride was then coupled to phenylacetic acid using General Procedure BG to provide the title compound.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.35 - 7.20 (m, 5H), 6.22 (bd, 1H), 4.83 (d, 1H), 4.65 (p, 1H), 3.68 (s, 3H), 3.55 (s, 2H), 2.21 (m, 1H), 1.40 (d, 3H), 0.97 (d, 3H), 0.93 (d, 3H).

¹³C-nmr (CDCl₃): δ = 173.25, 171.18, 170.22, 135.11, 129.94, 129.50, 127.88, 52.67, 48.49, 43.98, 30.53, 19.21, 18.75, 17.58.

Example B63

Synthesis of *N*-[(3-nitrophenyl)acetyl]-L-alanine *iso*-butyl ester

Following General Procedure BH above and using 3-nitrophenylacetic acid (Aldrich) and L-alanine *iso*-butyl ester hydrochloride (from Example BB above), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by recrystallization from butyl chloride.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 8.17 (m, 2H), 7.68 (d, 1H), 7.52 (t, 1H), 6.18 (m, 1H), 4.48 (m, 1H), 3.94 (m, 2H), 3.67 (s, 2H), 1.93 (m, 1H), 1.42 (d, 3H), 0.91 (d, 3H).

5 Optical Rotation: [α]₂₃ -49 (c 5, MeOH).

Example B64

Synthesis of *N*-[(3,5-difluorophenyl)acetyl]alanine ethyl ester

Following General Procedure BG and using 3,5-difluorophenylacetic acid
10 (Aldrich) and alanine ethyl ester (Aldrich), the title compound was prepared as a solid with a melting point of 93°-95°C. The reaction was monitored by tlc on silica gel (R_f = 0.8 in EtOAc) and purification was by chromatography on silica gel using EtOAc as the eluant followed by recrystallization from 1-chlorobutane.

NMR data was as follows:

15 ¹H-nmr (DMSO-*d*₆): δ = 1.30 (d, 3H); 3.52 (s, 2H).

C₁₃H₁₅NO₃F₂ (MW = 271.26, Mass Spectroscopy (MH⁺ 271)).

Example B65

Synthesis of *N*-[(3-nitrophenyl)acetyl]methionine ethyl ester

20 Following General Procedure BG above and using 3-nitrophenylacetic acid (Aldrich) and methionine ethyl ester hydrochloride (Aldrich), the title compound was prepared. The reaction was monitored by tlc on silica gel and purification was by recrystallization from butyl chloride.

NMR data was as follows:

25 ¹H-nmr (CDCl₃): δ = 8.18 (s, 1H), 8.15 (d, 1H) 7.66 (d, 1H), 7.48 (t, 1H), 6.30 (m, 1H), 4.67 (m, 1H), 4.21 (t, 2H), 3.67 (s, 2H), 2.47 (t, 2H), 2.12 (m, 2H), 2.08 (s, 3H), 1.27 (t, 3H).

Optical Rotation: [α]₂₃ -30 (c 5, MeOH).

30

Example B66

Synthesis of *N*-[(3-chlorophenyl)acetyl]alanine *iso*-butyl ester

Following General Procedure BG above and using 3-chlorophenylacetic acid (Aldrich) and alanine *iso*-butyl ester (prepared following General Procedure BJ above), the title compound was prepared. The reaction was monitored by tlc on silica gel.

5 NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.29 (m, 3H), 7.18 (m, 1H), 6.0 (m, 1H), 4.56 (m, 1H), 3.89 (m, 2H), 3.53 (s, 2H), 1.91 (m, 1H), 1.39 (d, 3 H), 0.91 (d, 3H).

Optical Rotation: [α]_D²⁵ -45 (c 5, MeOH).

C₁₅H₂₀NO₃Cl (MW = 297.78, Mass Spectroscopy (MH⁺ 297)).

10

Example B67

Synthesis of *N*-[(3-chlorophenyl)acetyl]alanine 2-(*N,N*-dimethylamino)ethyl ester

15 Following General Procedure BC above, and using *N*-(3-chlorophenyl-acetyl)alanine (from Example BD above) and 2-(*N,N*-dimethyl amino) ethanol (Aldrich), the title compound can be prepared. The reaction was monitored by tlc on silica gel and purification was by liquid chromatography using 0.1:2:0.79 NH₄OH:EtOH:CHCl₃ as the eluant.

NMR data was as follows:

20 ¹H-nmr (CDCl₃): 7.37 (s, 1H), 7.33-7.2 (m, 3H), 4.675-4.6 (m, 1H), 4.5-4.37 (m, 1H), 4.25-4.13 (m, 1H), 3.6 (d, *J* = 7 Hz, 2H), 2.86 (bs, 2H), 2.3 (s, 6H), 1.23 (d, *J* = 9 Hz, 3H).

C₁₅H₂₁N₂O₃Cl (MW = 313.799, Mass Spectroscopy (M⁺ 313)).

25

Example B68

Synthesis of 2-[(3,5-dichlorophenyl)acetamido]hexanoic acid methyl ester

Following General Procedure BF above, an using 3,5-dichlorophenylacetic acid (from Example BC above) and L-norleucine methyl ester hydrochloride (Bachem), the title compound was prepared as a solid having a melting point of
30 77°-78°C. The reaction was monitored by tlc on silica gel (R_f = 0.70 in 40% EtOAc/hexanes) and purification was by flash chromatography on silica gel using 40% EtOAc/hexanes as the eluant.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.20 (s), 7.18 (s), 6.6 (m), 4.55 (m), 3.7 (s), 3.5 (s), 3.4 (s), 2.0 (s), 1.8 (m), 1.6 (m), 1.2 (m), 0.8 (t).

¹³C-nmr (CDCl₃): δ = 173.54, 169.67, 138.43, 135.72, 128.33, 128.07,
5 78.04, 77.62, 77.19, 53.04, 52.90, 43.14, 32.57, 27.87, 22.81, 14.41.

Example B69

Synthesis of *N*-[(3,5-dichlorophenyl)acetyl]-L-alanine *iso*-butyl ester

Following General Procedure BF above, and using 3,5-dichlorophenylacetic
10 acid (from Example BC above) and L-alanine *iso*-butyl ester hydrochloride
(from Example BB above), the title compound was prepared as a solid having a
melting point of 115°-116°C. The reaction was monitored by tlc on silica gel
(R_f = 0.40 in 3% methanol/dichloromethane) and purification was by flash
chromatography on silica gel using 3% methanol/dichloromethane as the eluant.

15 NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.27 (d, *J* = 2 Hz, 1H), 7.19 (s, 2H), 6.22 (d, *J* = 6
Hz, 1H), 4.59 (quint., *J* = 7 Hz, 1H), 3.9 (q, *J* = 4 Hz, 2H), 3.5 (s, 2H), 1.9 (m,
1H), 1.4 (d, *J* = 7 Hz, 3H), 0.91 (d, *J* = 7 Hz, 6H).

¹³C-nmr (CDCl₃): δ = 173.45, 169.37, 138.31, 135.75, 128.39, 128.11,
20 78.04, 77.61, 77.19, 72.19, 54.03, 48.97, 43.12, 28.24, 19.52, 19.49, 19.09.

C₁₅H₁₉NO₃Cl₂ (MW = 331.9, Mass Spectroscopy (MH⁺ 332)).

Example B70

Synthesis of *N*-(cyclohexylacetyl)-L-alanine *iso*-butyl ester

25 Following General Procedure BB above, and using cyclohexylacetic acid
(Aldrich) and L-alanine *iso*-butyl ester hydrochloride (from Example BB above),
the title compound was prepared as a solid having a melting point of 92°C-
93°C. The reaction was monitored by tlc on silica gel (R_f = 0.39 in 1:3
EtOAc:hexane) and purification was by extraction with Et₂O followed by washes
30 with aqueous K₂CO₃ and aqueous HCl.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 0.93 (d, *J* = 6.7 Hz, 6H), 0.85-1.01 (m, 2H), 1.05-1.35 (m, 3H), 1.40 (d, *J* = 7.1 Hz, 3H), 1.60-1.85 (m, 6H), 1.95 (m, 1H), 2.06 (d, *J* = 7.0 Hz, 2H), 3.92 (m, 2H), 4.61 (m, 1H), 6.08 (bd, 1H).

¹³C-nmr (CDCl₃): δ = 18.7, 18.9, 26.0, 26.1, 27.6, 33.0, 35.3, 44.6, 47.9, 71.4, 171.8, 173.3.

C₁₅H₂₇NO₃ (MW = 269.39, Mass Spectroscopy (MH⁺ 270)).

Example B71

Synthesis of *N*-(cyclopentylacetyl)-L-alanine *iso*-butyl ester

Following General Procedure BB above, and using cyclopentylacetic acid (Aldrich) and L-alanine *iso*-butyl ester hydrochloride (from Example BB above), the title compound was prepared as a solid having a melting point of 62°C-64°C. The reaction was monitored by tlc on silica gel (R_f = 0.37 in 1:3 EtOAc:hexane) and purification was by extraction with Et₂O followed by washes with aqueous K₂CO₃ and aqueous HCl.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 0.87 (d, *J* = 6.8 Hz, 6H), 1.01-1.17 (m, 2H), 1.34 (d, *J* = 7.2 Hz, 3H), 1.40-1.62 (m, 4H), 1.70-1.83 (m, 2H), 1.89 (m, 1H), 2.15 (m, 3H), 3.86 (m, 2H), 4.55 (m, 1H), 6.30 (d, *J* = 7.1 Hz, 1H).

¹³C-nmr (CDCl₃): δ = 18.4, 18.78, 18.80, 24.8 (very high), 27.5, 32.27, 32.32, 36.9, 42.5, 47.7, 71.2, 172.2, 173.2.

Elemental Analysis-Calcd (%): C, 65.85; H, 9.87; N, 5.49; Found (%): C, 66.01; H, 10.08; N, 5.49.

C₁₄H₂₅NO₃ (MW = 255.36, Mass Spectroscopy (MH⁺ 256)).

Example B72

Synthesis of *N*-[(cyclohex-1-enyl)acetyl]-L-alanine *iso*-butyl ester

Following General Procedure BB above, and using cyclohex-1-enyl acetic acid (Alfa) and L-alanine *iso*-butyl ester hydrochloride (from Example BB above), the title compound was prepared as a solid having a melting point of 49°C-51°C. The reaction was monitored by tlc on silica gel (R_f = 0.40 in 1:3

EtOAc:hexane) and purification was by extraction with Et₂O followed by washes with aqueous K₂CO₃ and aqueous HCl.

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 0.91 (d, *J* = 4.5 Hz, 3H), 0.93 (d, *J* = 6.7 Hz, 3H),
5 1.40 (d, *J* = 7.2 Hz, 3H), 1.52-1.70 (m, 4H), 1.97 (m, 3H), 2.06 (bs, 2H), 2.89
(s, 2H), 3.92 (m, 2H), 4.59 (m, 1H), 5.65 (s, 1H), 6.33 (d, *J* = 6.6 Hz, 1H).

¹³C-nmr (CDCl₃): δ = 18.7, 18.91, 18.93, 21.9, 22.7, 25.3, 27.6, 28.3, 46.1,
47.9, 71.4, 127.1, 132.5, 170.6, 173.1.

Elemental Analysis-Calc (%): C, 67.38; H, 9.42; N, 5.24; Found (%): C,
10 67.34; H, 9.54; N, 5.16.

C₁₅H₂₅NO₃ (MW = 267.37, Mass Spectroscopy (MH⁺ 268)).

Example B73

Synthesis of *N*-[(3-chlorophenyl)acetyl]alanine 3-methylbut-2-enyl thioester

15 Following General Procedure BC above, and using *N*-[(3-chlorophenyl)acetyl] alanine and 3-methyl-2-butene thioester (TCI), the title compound can be prepared. The reaction was monitored by tlc on silica gel and purification was by liquid chromatography using 3:7 EtOAc:Hexane as the eluant.

20 NMR data was as follows:

¹H-nmr (DMSO-*d*₆): δ = 5.2-5.075 (m, 1H), 4.37 (dq, *J* = 9 Hz, 1H), 3.56
(s), 3.43 (d, *J* = 12 Hz, 2H), 1.266 (d, *J* = 12 Hz, 6H) 1.3 (d, *J* = 9 Hz, 3H).

C₁₆H₂₀NO₂ClS (MW = 325.86, Mass Spectroscopy (M⁺ 325)).

25

Example B74

Synthesis of *N*-[(2-phenyl)-2-fluoroacetyl]alanine ethyl ester

Following General Procedure BF above, and using α-fluorophenyl acetic acid (Aldrich) and alanine ethyl ester (Aldrich), the title compound was prepared. The reaction was monitored by tlc on silica gel (R_f = 0.75 in 1:1
30 EtOAc:hexane) and purification was by chromatography on silica gel using 1:2 ethyl acetate/hexanes as the eluent.

NMR data was as follows:

¹H-nmr (DMSO-*d*₆): δ = 1.14 (q, 3H), 1.34 (d, 3H), 4.07 (m, 2H), 4.33 (m, 1H), 5.84 (d, 1H), 6.01 (d, 1H), 7.40-7.55 (m, 5H), 8.87 (m, 1H).

C₁₃H₁₆NO₃F (MW = 253.27, Mass Spectroscopy (MH⁺ 253)).

5

Example B75

Synthesis of *N*-(3,5-difluorophenylacetyl)-L-phenylglycine methyl ester

Following General Procedure BF above, and using 3,5-difluorophenylacetic acid (Aldrich) and L-phenylglycine methyl ester hydrochloride (Bachem), the title compound was prepared.

10

NMR data was as follows:

¹H-nmr (CDCl₃): δ = 7.4-7.3 (m, 5H), 6.9-6.7 (m, 3H), 6.55 (d 1H, 7.1 Hz), 5.56 (d 1H 7 Hz), 3.72 (s 3H), 3.57 (s 2H)

¹³C-nmr (CDCl₃): δ = 197.6, 177.6, 171.8, 169.3, 136.7, 129.6, 129.3, 127.8, 113.0, 112.9, 112.7, 111.4, 103.8, 103.5, 65.1, 57.2, 53.5, 45.1, 43.3, 43.3

15

C₁₇H₁₅NO₃F₂ (MW = 319.31, Mass Spectroscopy (MH⁺ 320)).

Example B76

20 Synthesis of *N*-(3,5-difluorophenylacetyl)-L-phenylglycine *iso*-butyl ester

The 3,5-difluorophenylacetic acid (Aldrich) was EDC coupled to L-phenylglycine methyl ester hydrochloride (Bachem) via General Procedure BF above.

The resulting compound was placed in a large excess of the desired alcohol. A catalytic amount of dry NaH was added, and the reaction was followed by tlc until the presence of starting material was no longer detected. The reaction was quenched with a few milliliters of 1N HCl, and after a few minutes of stirring saturated aqueous NaHCO₃ was added. The volume of the reaction mixture was reduced on a rotary evaporator until the excess alcohol was removed and then the remaining residue was taken up in ethyl acetate and additional water was added. The organic phase was washed with saturated aqueous NaCl and dried

25

30

over MgSO_4 . The solution was stripped free of solvent on a rotary evaporator, and the crude product residue was then further purified by chromatography.

NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 7.35\text{--}7.3$ (m 5H), 6.8-6.7 (m 3H) 6.60 (d 1H, 7 Hz),
5 5.55 (d 1H 7.1 Hz), 3.9 (m 2H), 3.60 (s 2H), 1.85 (m 1H 7 Hz), 0.8 (q 6H 7 Hz)

^{13}C -nmr (CDCl_3): $\delta = 171.3, 169.3, 165.4, 138.5, 137.0, 129.5, 129.2,$
127.6, 113.1, 113.0, 112.8, 112.7, 103.8, 103.5, 103.2, 75.5, 57.2, 43.4, 43.3,
28.2, 19.3

10 $\text{C}_{20}\text{H}_{21}\text{NO}_3\text{F}_2$ (MW = 361.39, Mass Spectroscopy (MH +362)).

Example B77

Synthesis of *N*-(cyclopentylacetyl)-L-phenylglycine methyl ester

Following General Procedure BD above, and using cyclopentylacetic acid
15 (Aldrich) with L-phenylglycine methyl ester hydrochloride (Bachem) the title compound was prepared.

NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 7.35$ (s, 5H), 6.44 (bd, 1H), 5.6 (d, 1H), 3.72 (s, 3H),
2.24 (bs, 3H), 1.9-1.4 (m, 6H), 1.2-1.05 (m, 2H)

20 ^{13}C -nmr (CDCl_3): $\delta = 172.3, 171.7, 136.7, 129.0, 128.6, 127.3, 56.2, 52.7,$
42.5, 36.9, 32.40, 32.38, 24.8

Example B78

Synthesis of *N*-(cyclopentylacetyl)-L-alanine methyl ester

25 Following General Procedure BD above, and using cyclopentylacetic acid (Aldrich) with L-alanine methyl ester hydrochloride (Sigma) the title compound was prepared.

NMR data was as follows:

30 ^1H -nmr (CDCl_3): $\delta = 6.38$ (d, 1H), 4.50 (m, 1H), 3.65 (s, 3H), 2.13 (bs, 3H), 1.80-1.00 (m (includes d at 1.30, 3H), 11H)

^{13}C -nmr (CDCl_3): $\delta = 173.7, 172.5, 52.1, 47.6, 42.3, 36.8, 32.15, 32.14, 18.0$

$\text{C}_{11}\text{H}_{19}\text{NO}_3$ (MW = 213.28, Mass Spectroscopy (MH^+ 214)).

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Example B79

Synthesis of *N*-(cyclopropylacetyl)-L-phenylglycine methyl ester

Following General Procedure BD above, and using cyclopropylacetic acid (Aldrich) with L-phenylglycine methyl ester hydrochloride (Bachem), the title compound was prepared.

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NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 7.35$ (m, 5H) 6.97 (bd, $J = 7.2$ Hz, 1H) 5.59 (d, $J = 7.8$ Hz, 1H), 3.71 (s, 3H), 2.17 (m, 2H), 1.05-0.95 (m, 1H), 0.62 (m, 2H), 0.02 (m, 2H)

15

^{13}C -nmr (CDCl_3): $\delta = 171.9, 174.6, 136.6, 129.0, 128.5, 127.2, 56.1, 52.7, 41.0, 6.9, 4.37, 4.33$

Example B80

Synthesis of *N*-(cyclopropylacetyl)-L-alanine methyl ester

Following General Procedure BD above, and using cyclopropylacetic acid (Aldrich) with L-alanine methyl ester hydrochloride (Sigma), the title compound was prepared.

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NMR data was as follows:

^1H -nmr (CDCl_3): $\delta = 6.60$ (d, 1H), 4.55 (m, 1H), 3.69 (s, 3H), 2.10 (m, 2H), 1.34 (d, 3H), 0.95 (m, 1H), 0.58 (m, 2H) 0.15 (m, 2H)

25

^{13}C -nmr (CDCl_3): $\delta = 173.7, 172.3, 52.3, 47.7, 41.0, 18.2, 6.7, 4.27, 4.22$

Example B81

Synthesis of *N*-[(3-nitrophenyl)acetyl]-L-methionine *iso*-butyl ester

Following General Procedure BH above, and using nitrophenylacetic acid (Aldrich) and L-methionine (Aldrich), the title compound was prepared as a tan oil. The reaction was monitored by tlc on silica gel.

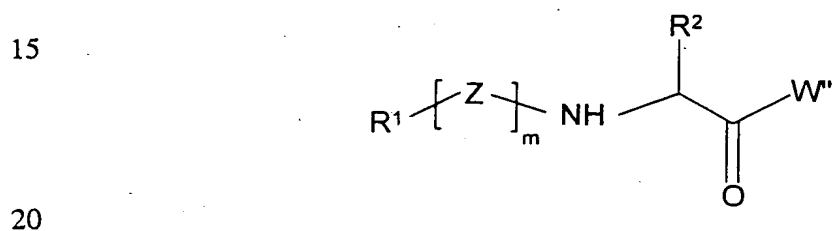
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NMR data was as follows:

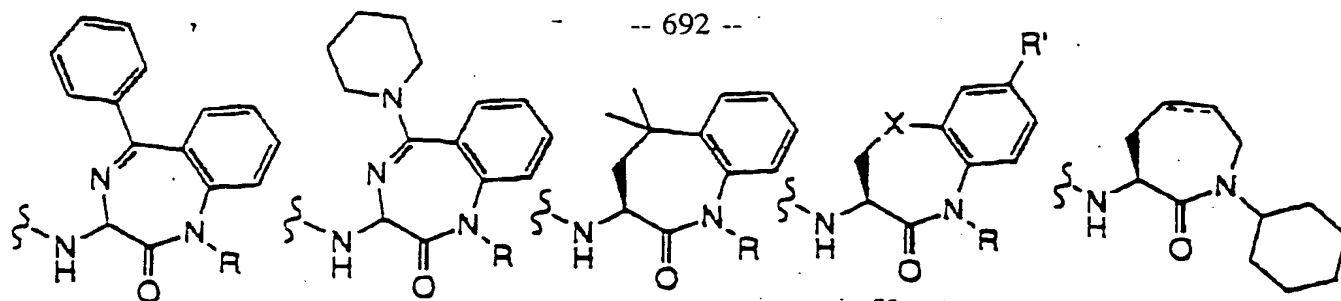
^1H -nmr (CDCl_3): δ = 8.16 (m, 2H) 7.67 (d, 1H) 7.32 (t, 1H), 6.31 (bd, 1H), 4.69 (m, 1H), 3.90 (d, 2H), 3.68 (s, 2H), 2.47 (t, 2H), 2.15 (m, 1H), 2.02 (s, 3H), 1.90 (m, 2H), 0.91 (d, 6H).

5 $\text{C}_{17}\text{H}_{24}\text{N}_2\text{O}_5\text{S}$ (MW = 368.4, Mass Spectroscopy (MH^+ 368)).

Additionally, each of the carboxylic acids described above (or the carboxylic acids prepared by hydrolysis of the above carboxylic acid esters) could be coupled with an appropriate α -aminolactam to provide for compounds
10 of the formula:

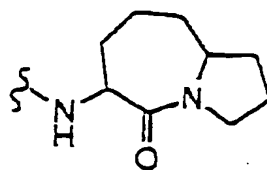
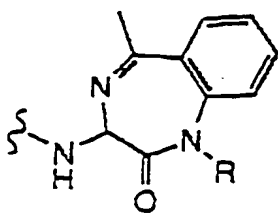
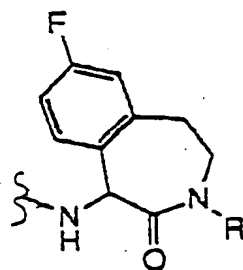
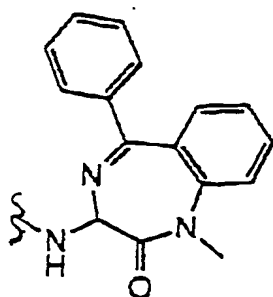
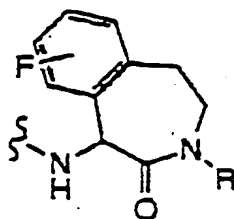


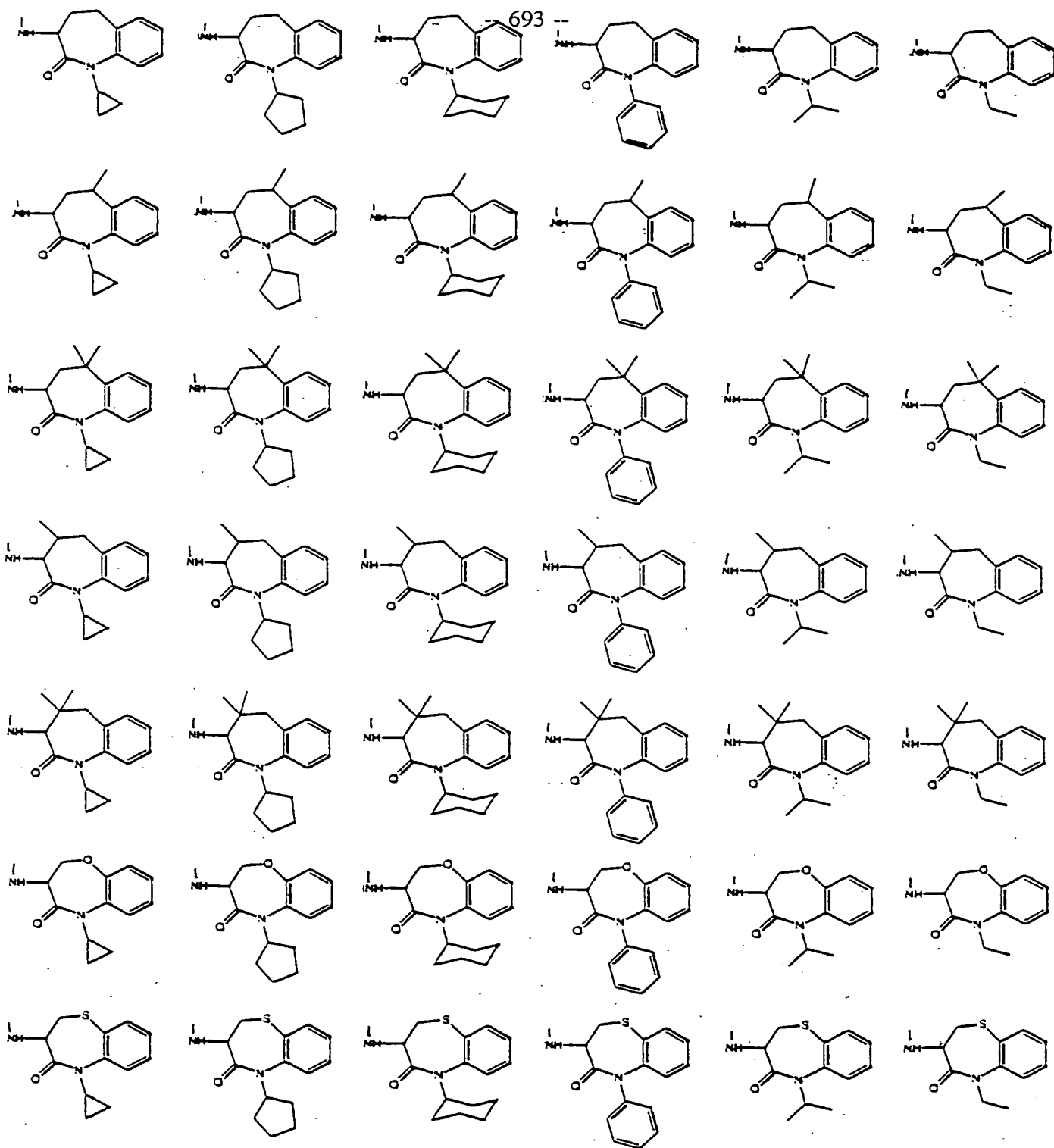
25 where $\text{R}^1\text{-[Z]}_m\text{-NH-CHR}^2\text{-C(O)-}$ is the residue of the carboxylic acid (i.e., R^1 , R^2 , Z , and m are as defined above) and W'' is selected from the following structures:

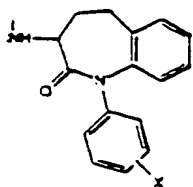
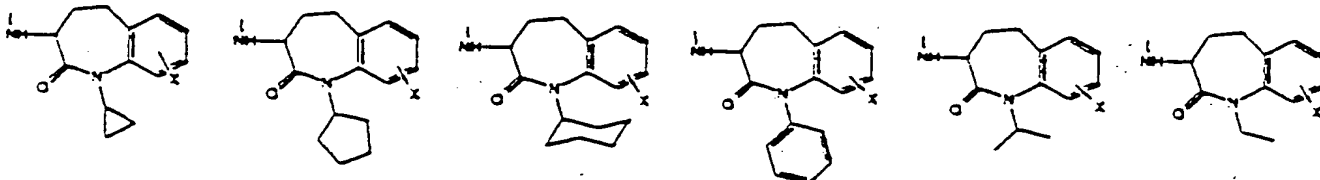
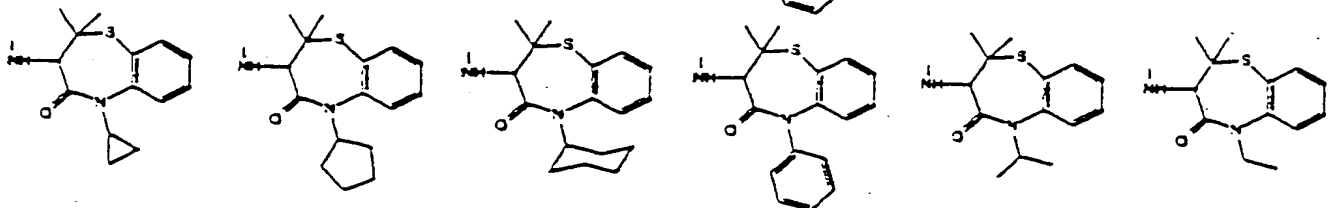
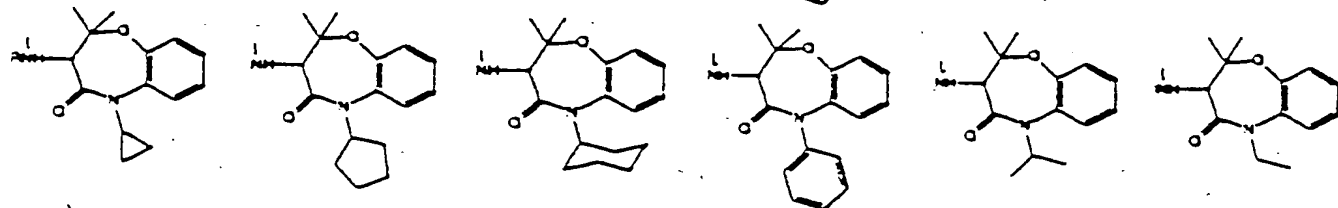
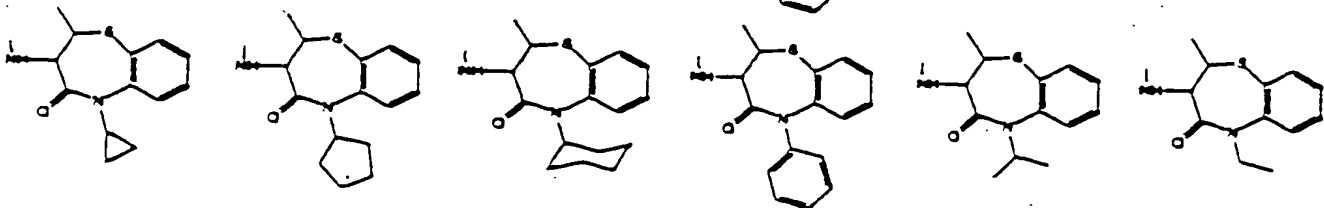
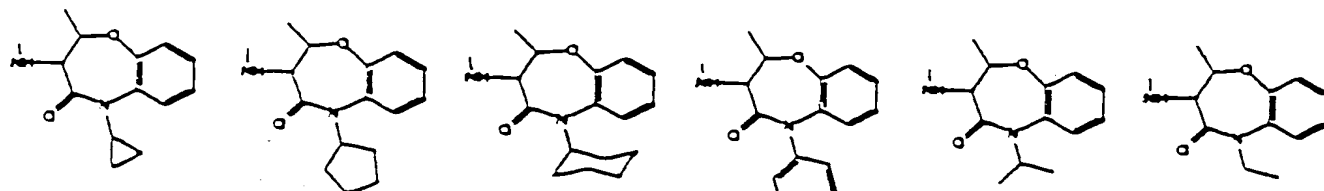


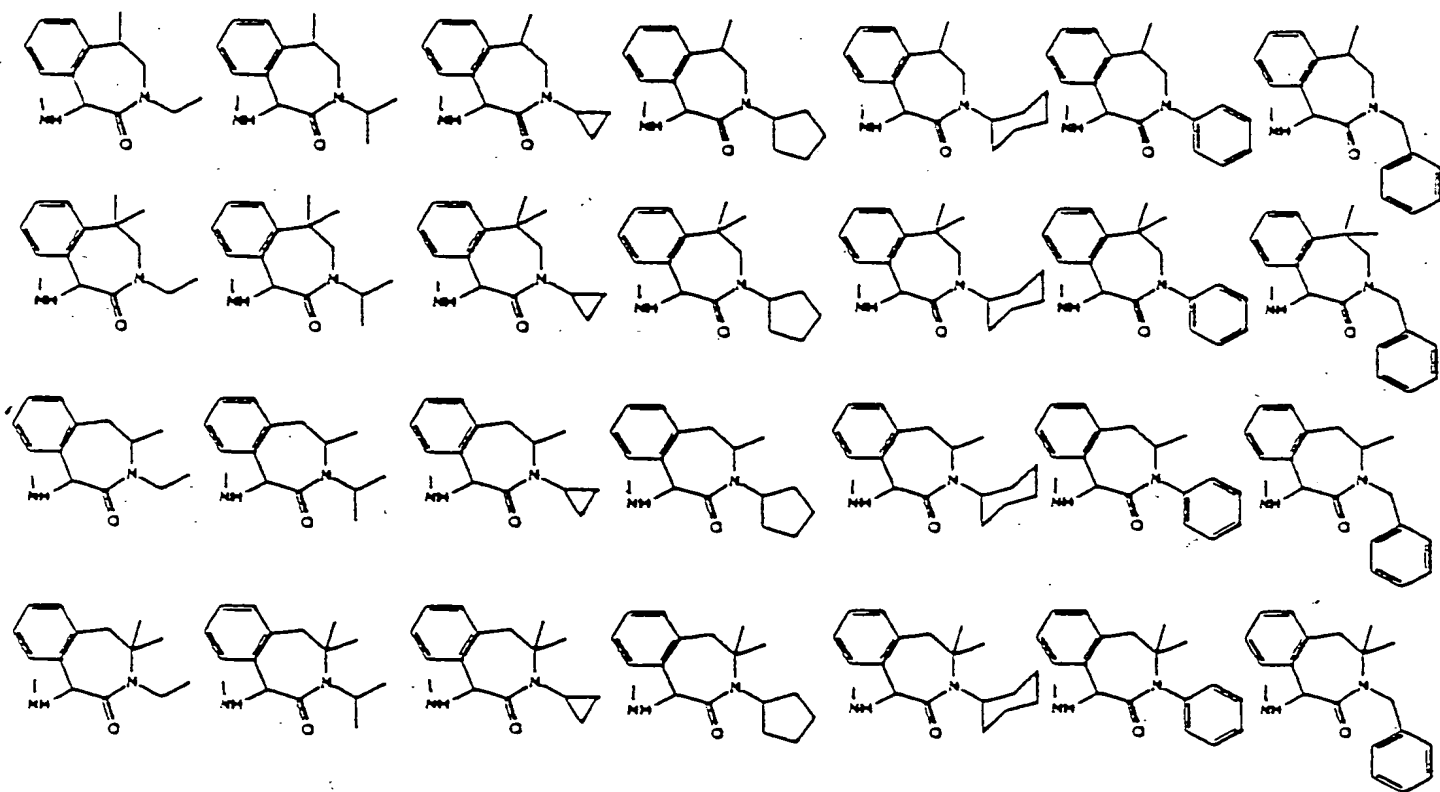
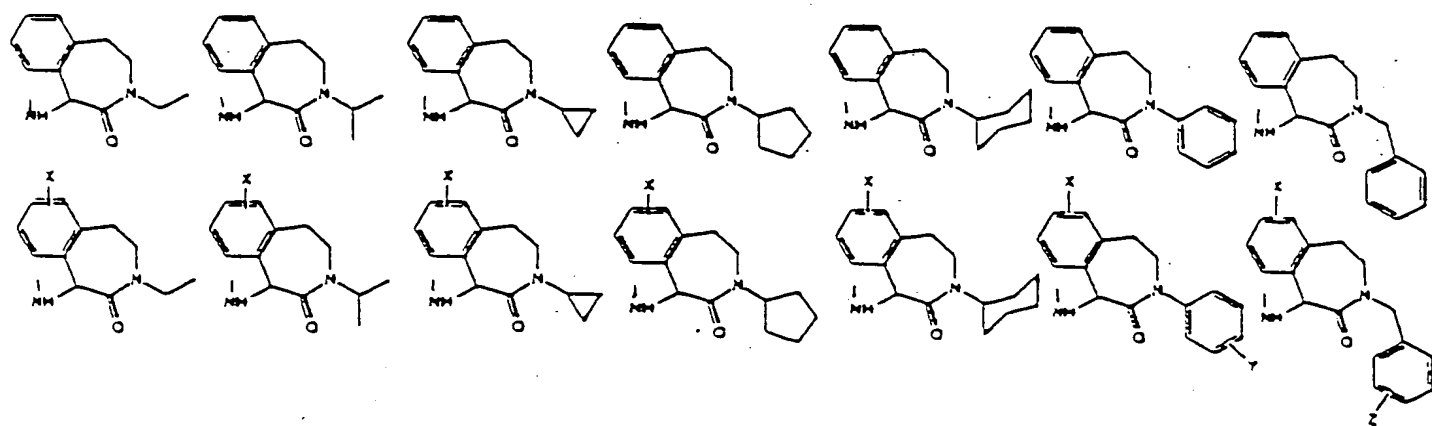
R = H, Et

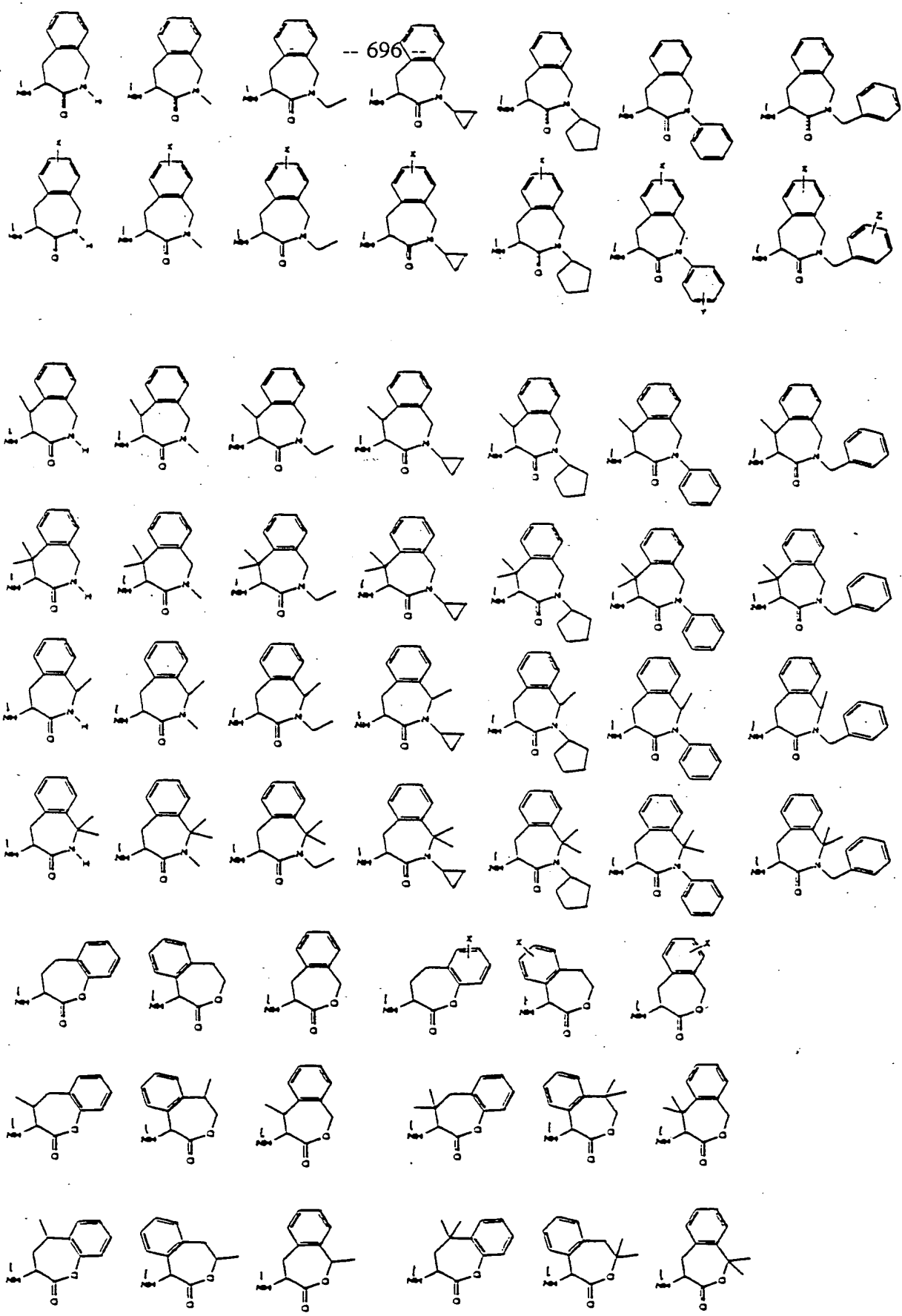
X = SO₂, R' = H
X = O, R' = F

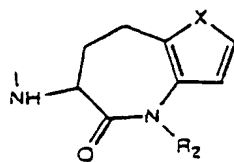
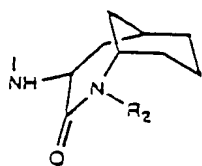
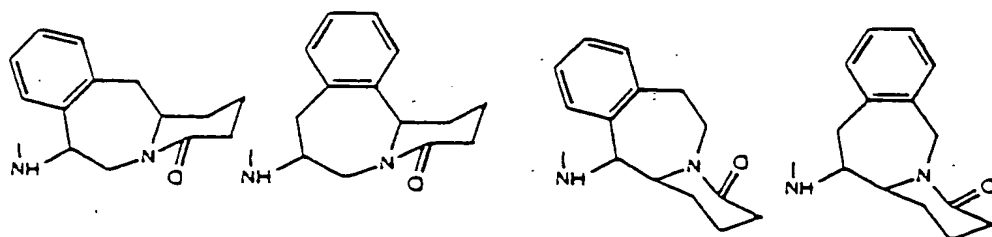




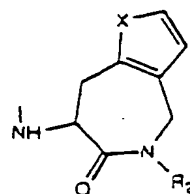




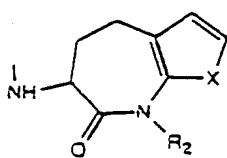




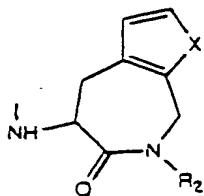
X=O.S



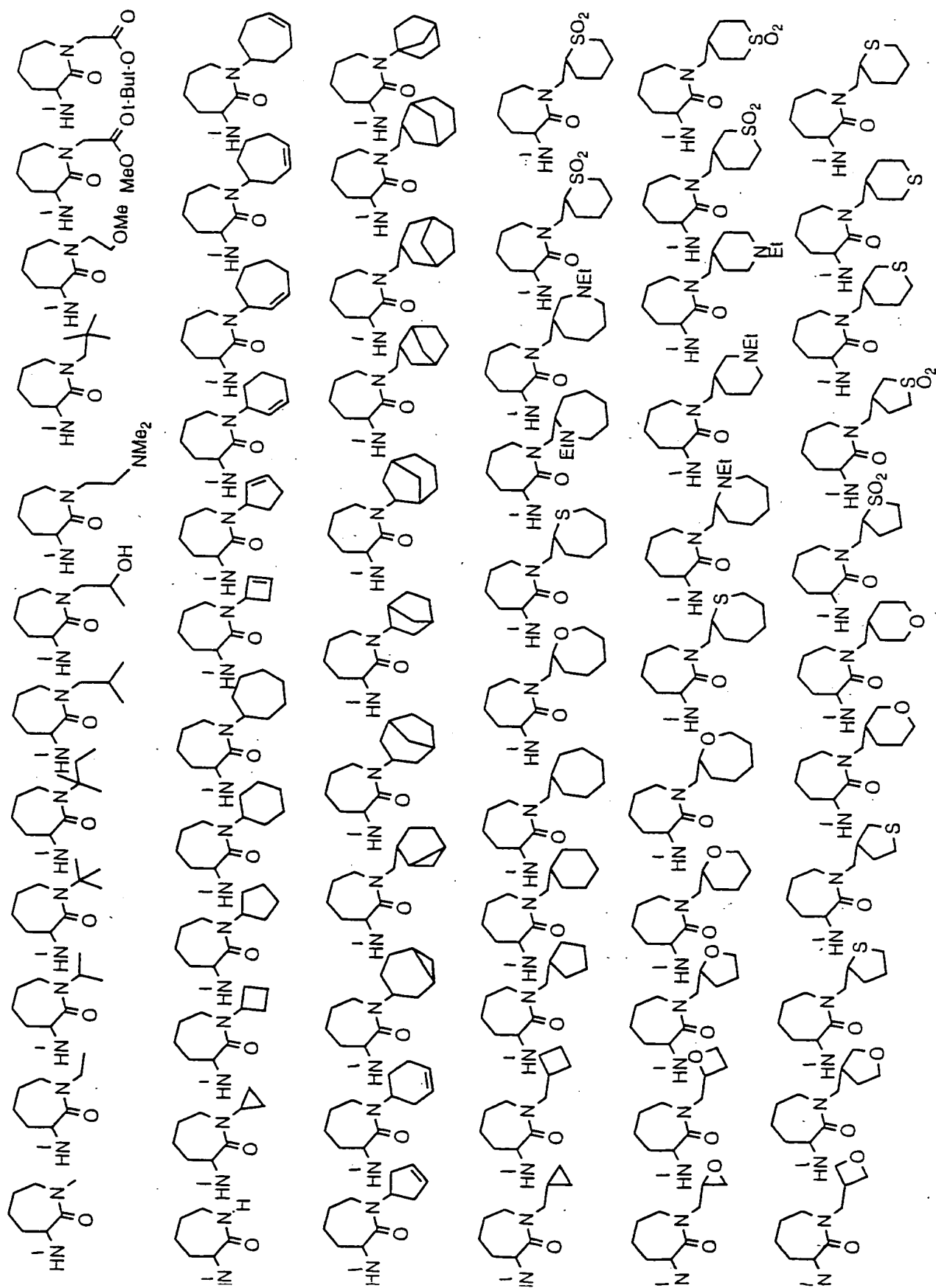
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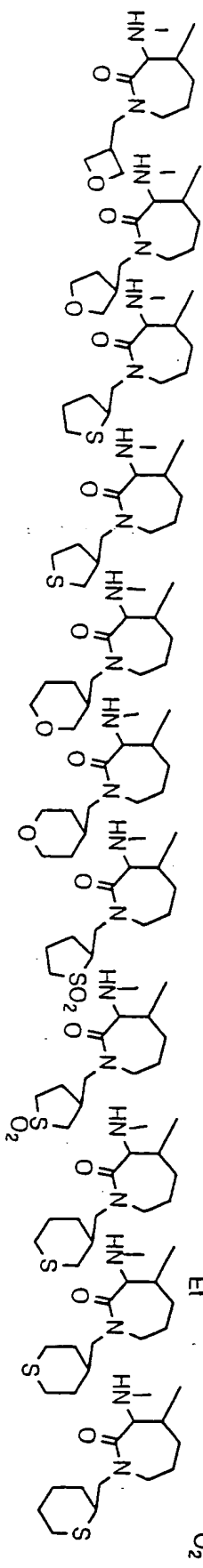
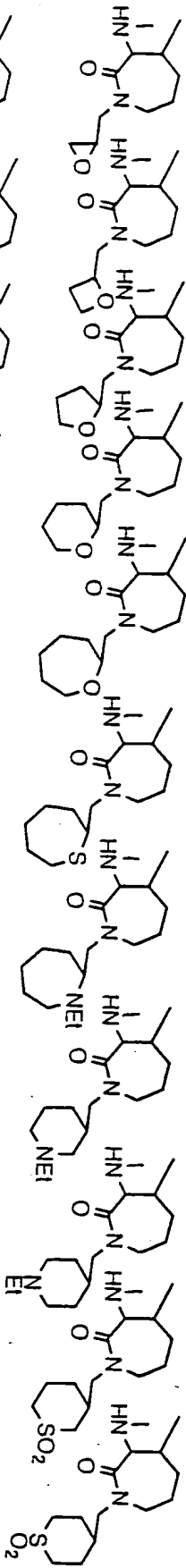
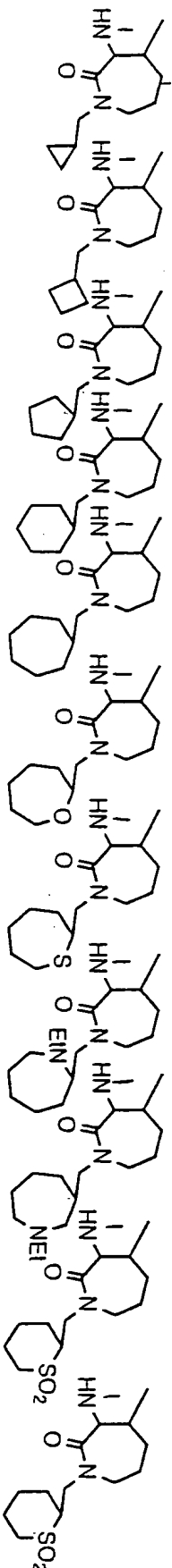
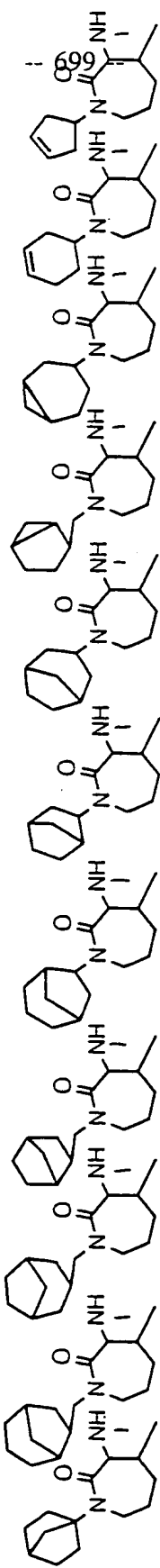
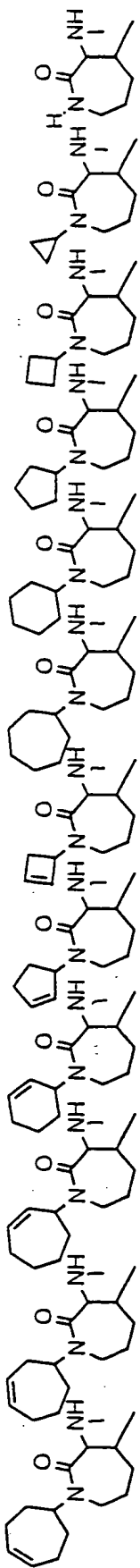
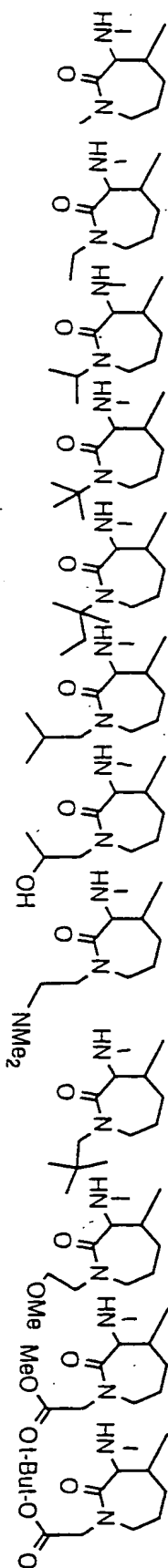


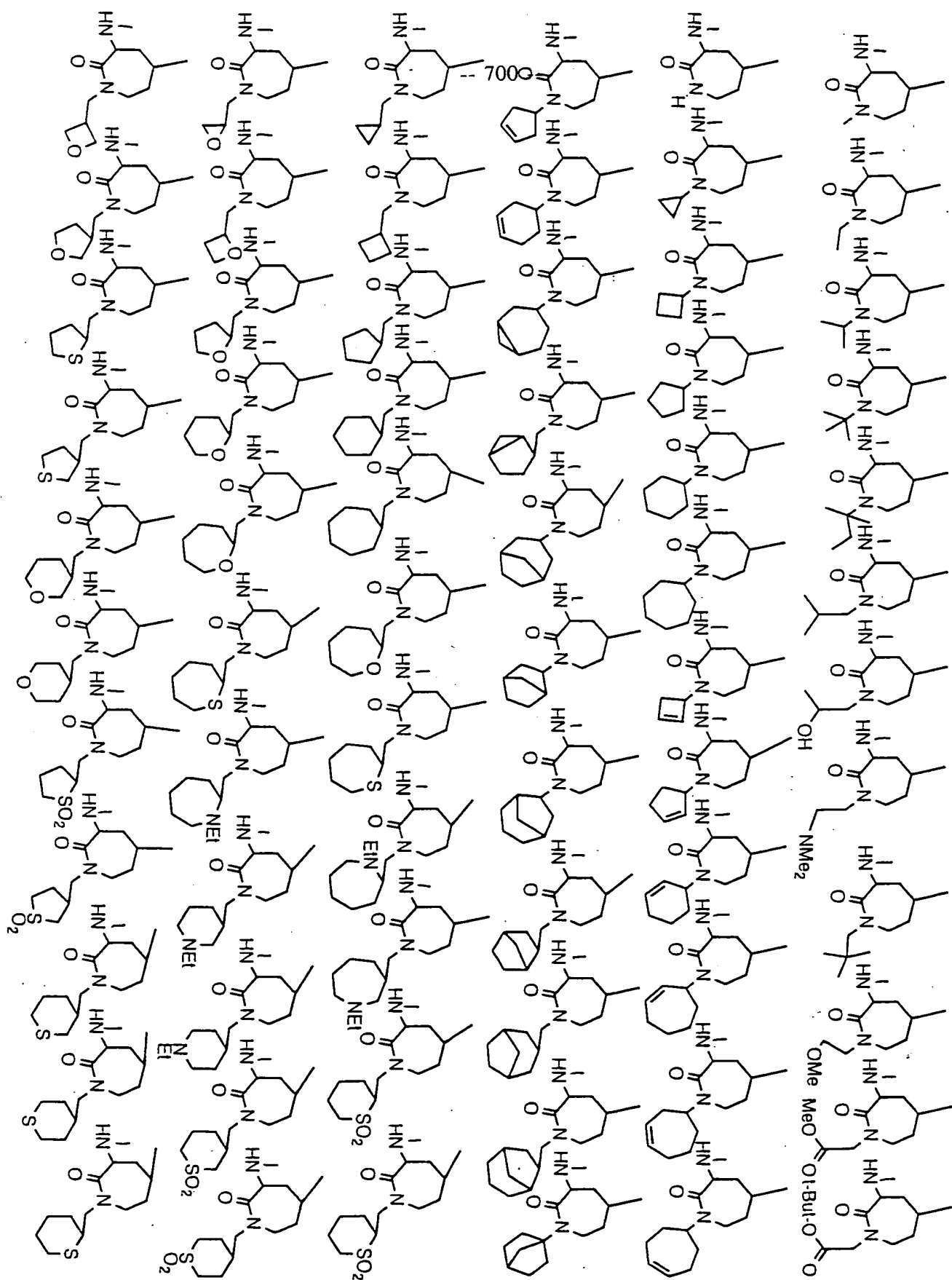
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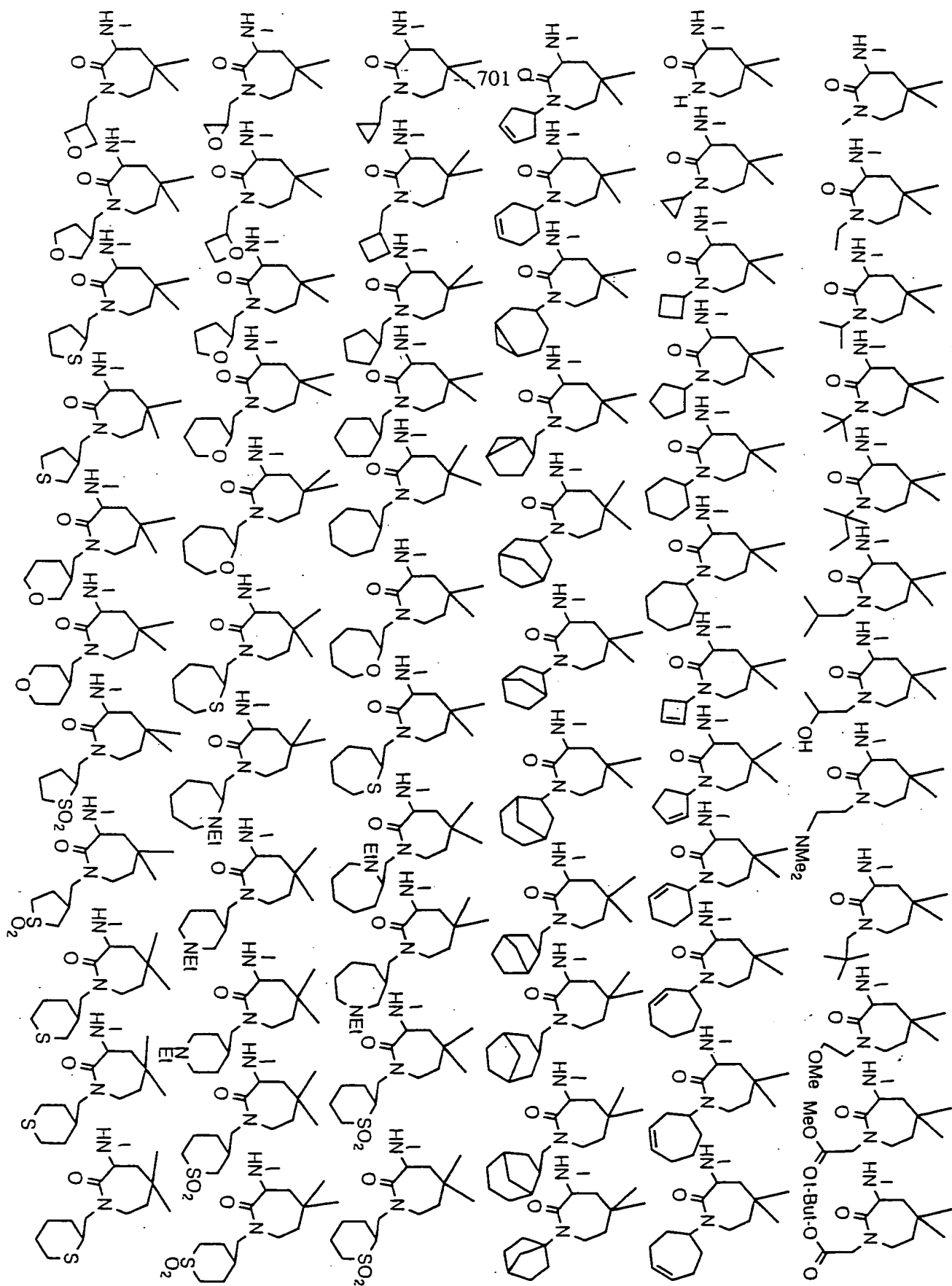


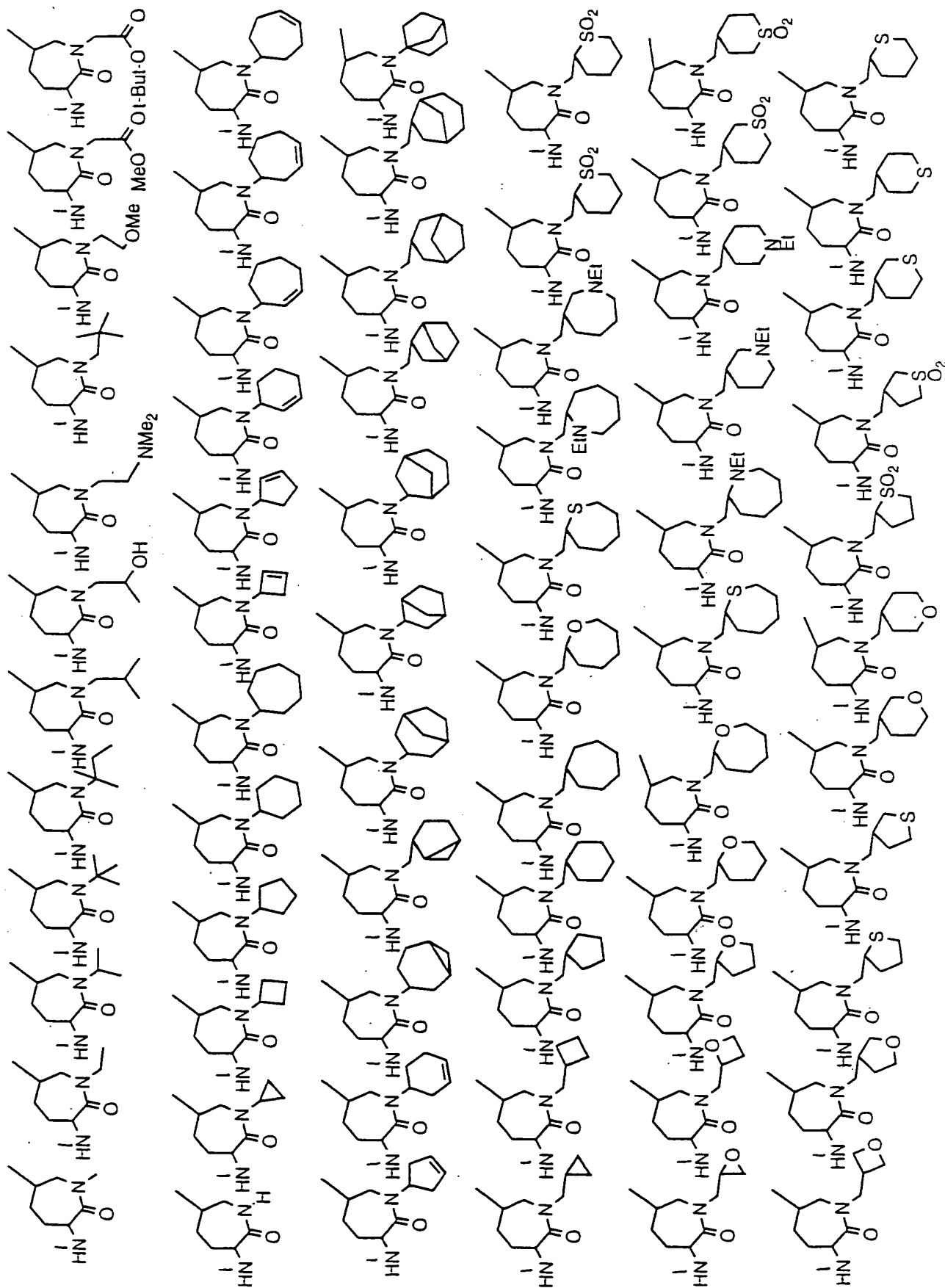
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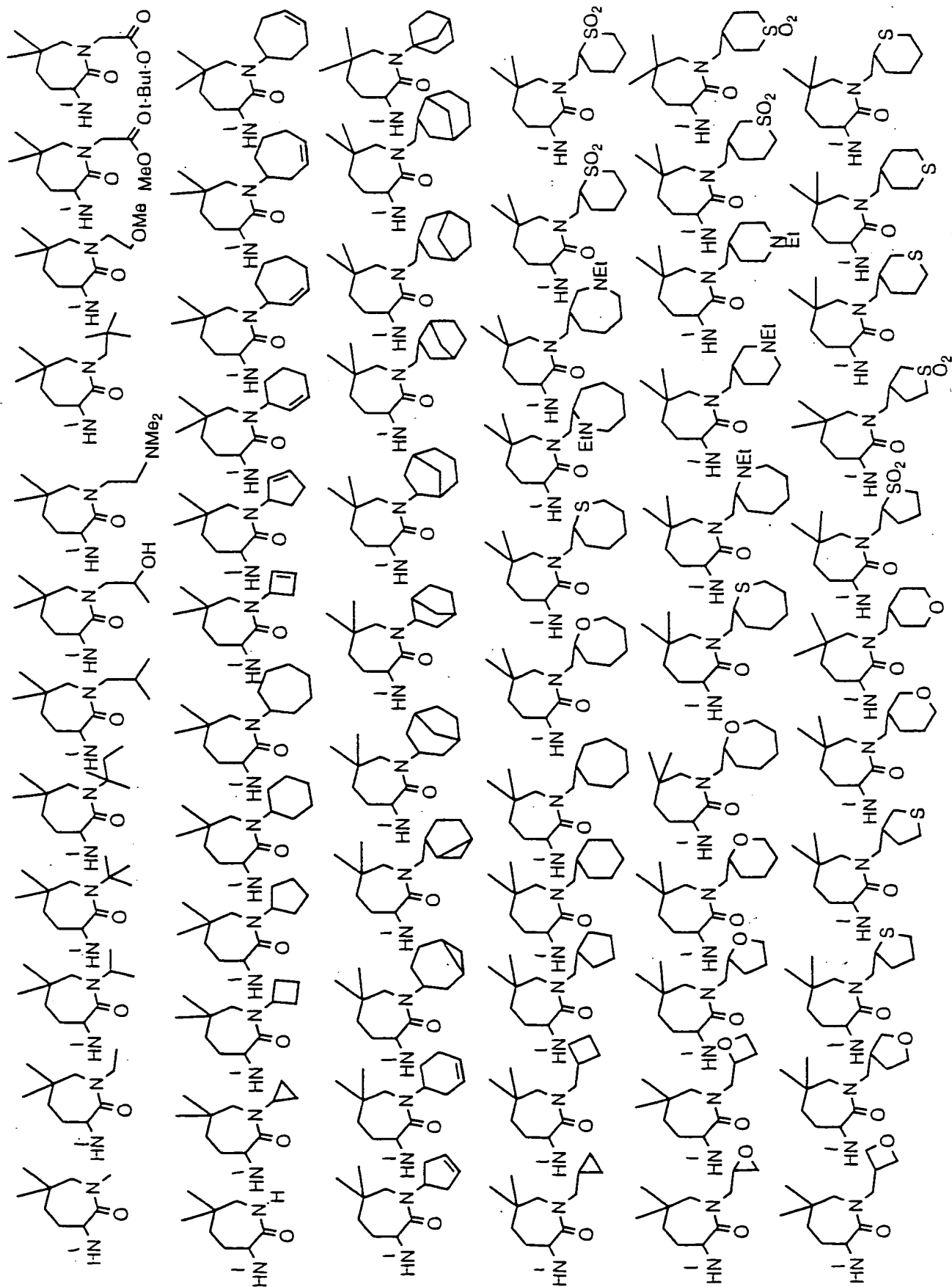


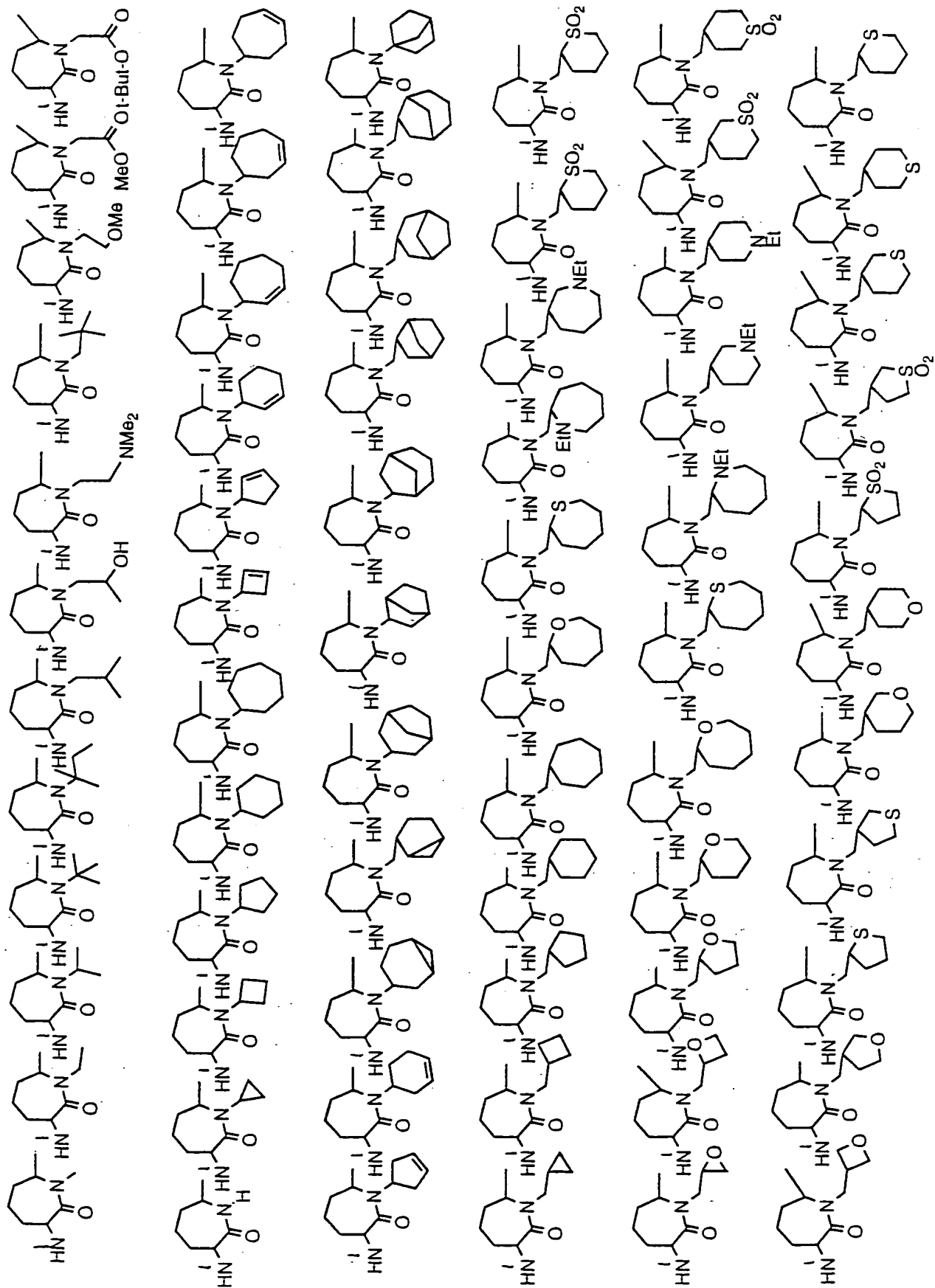


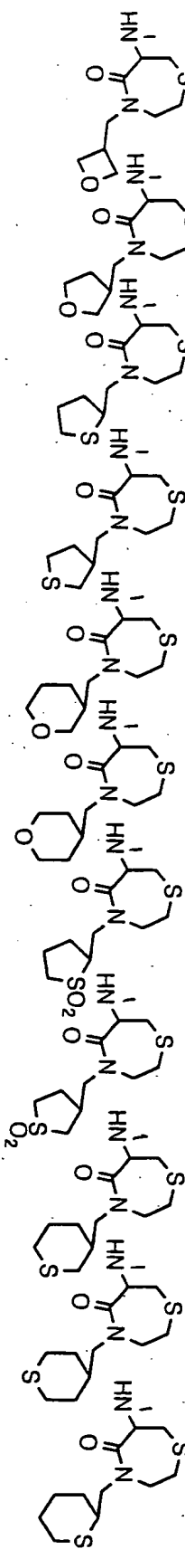
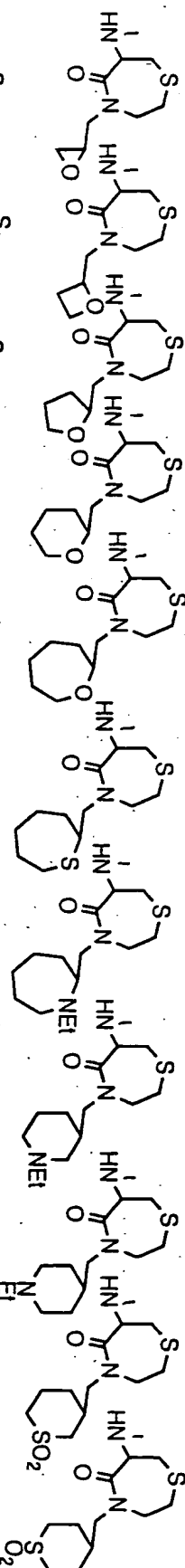
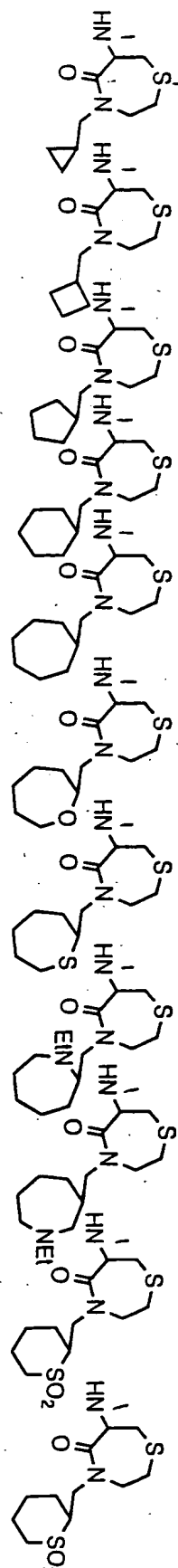
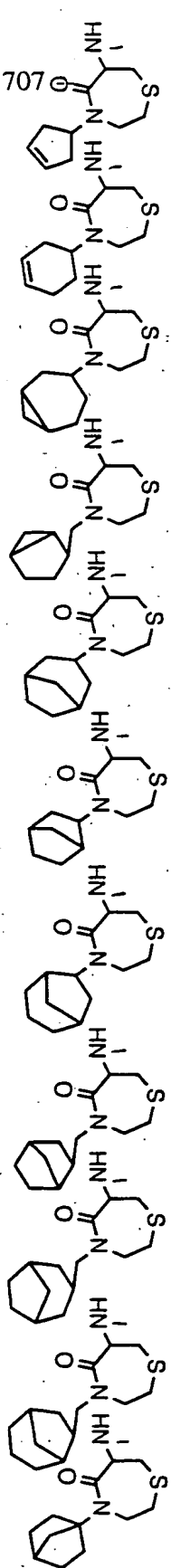
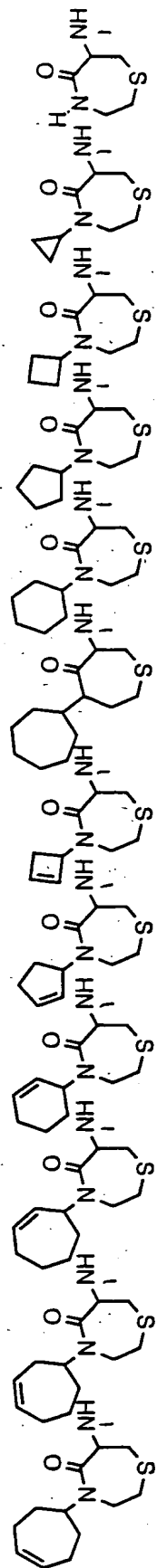
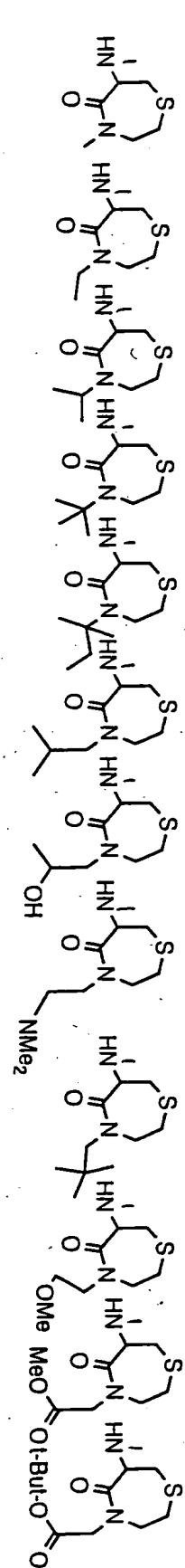


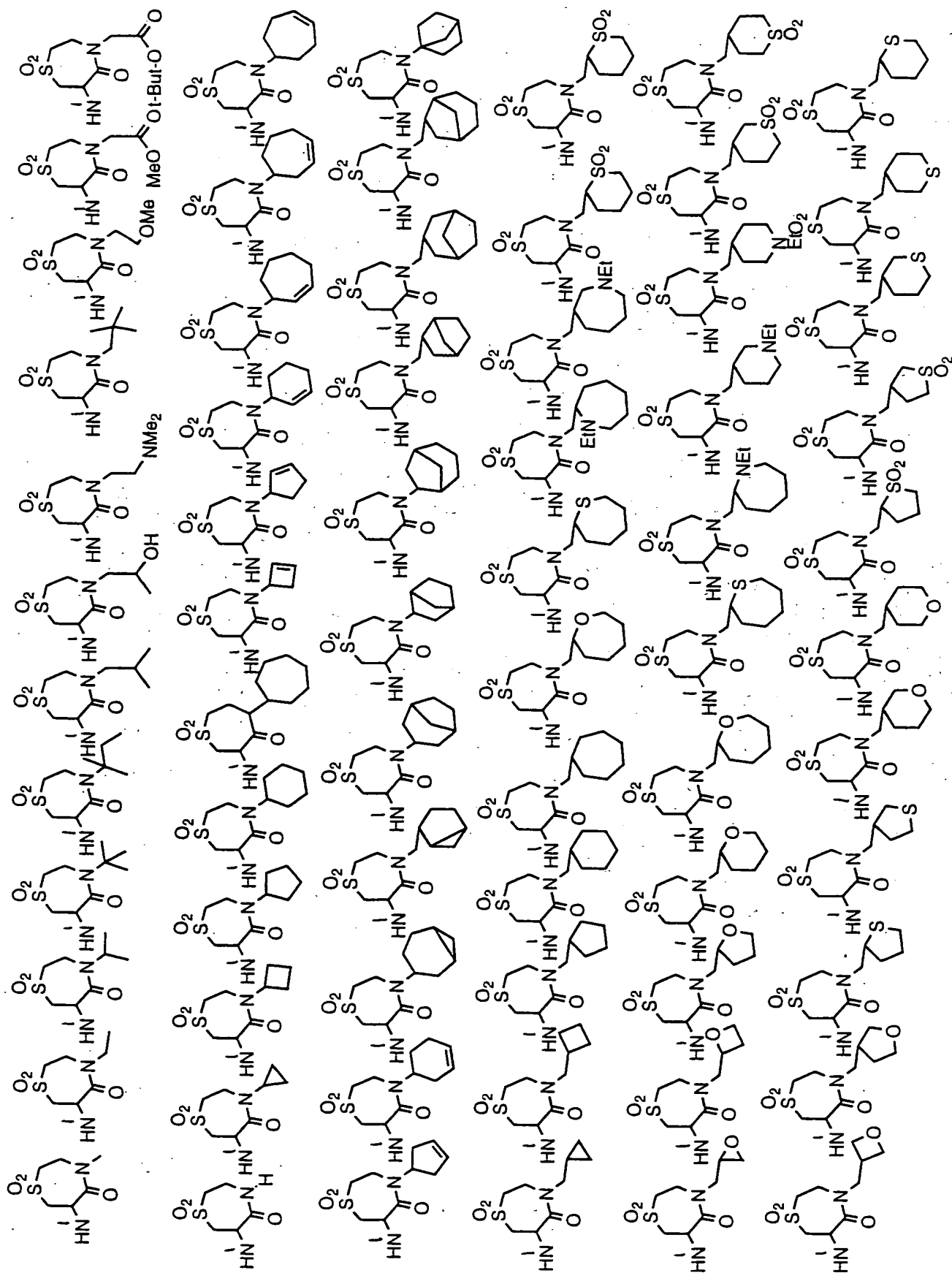


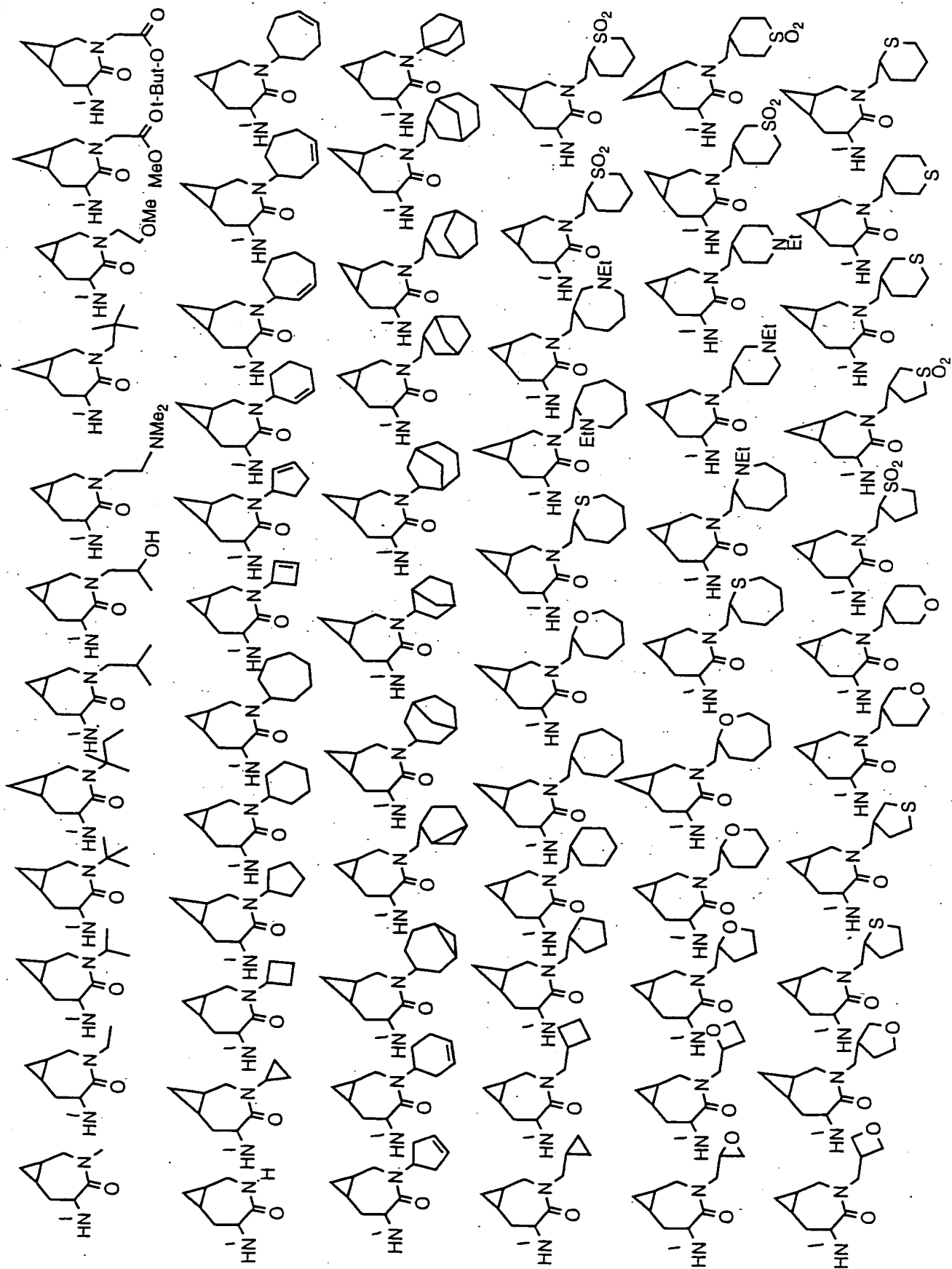


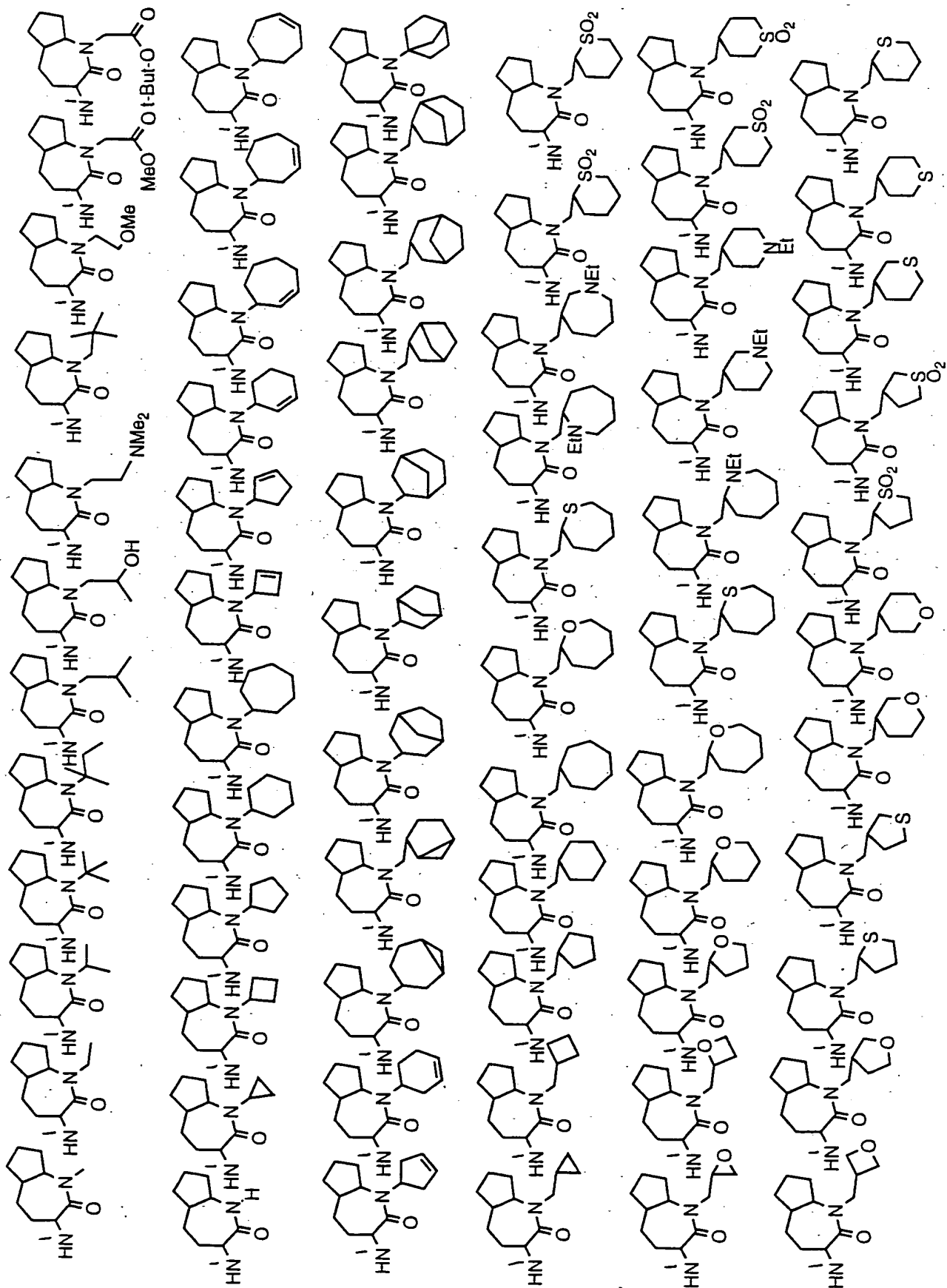


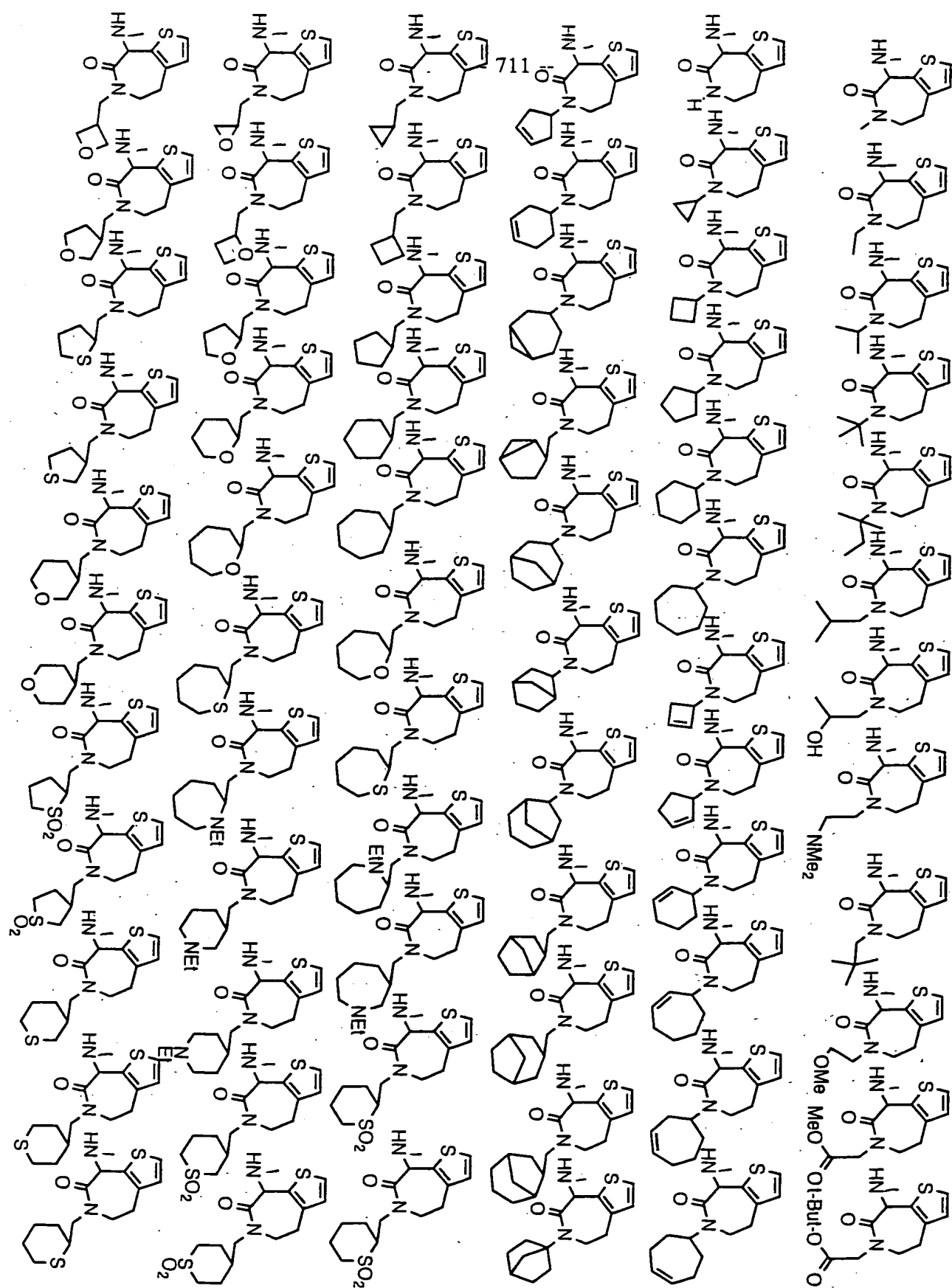


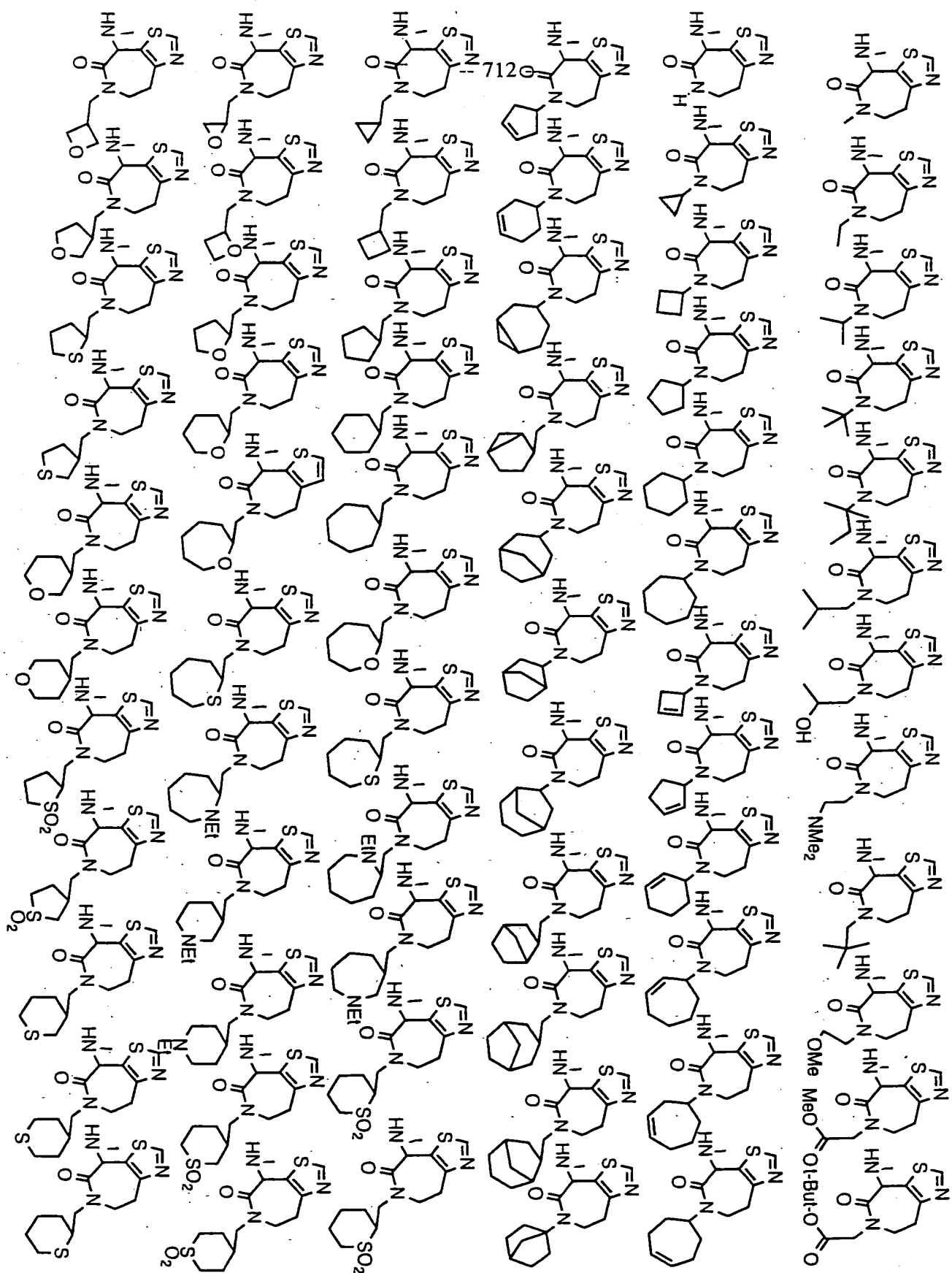


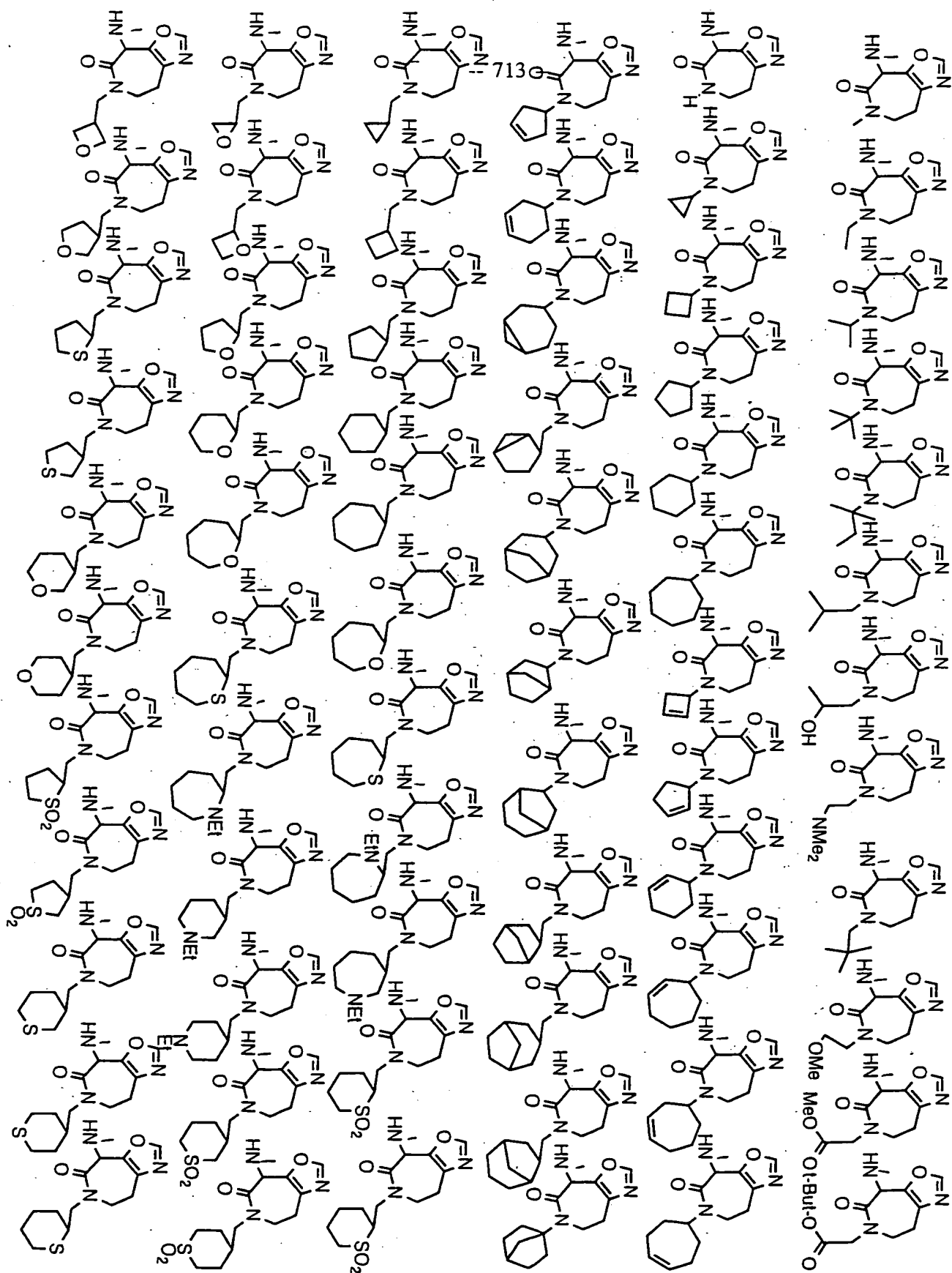


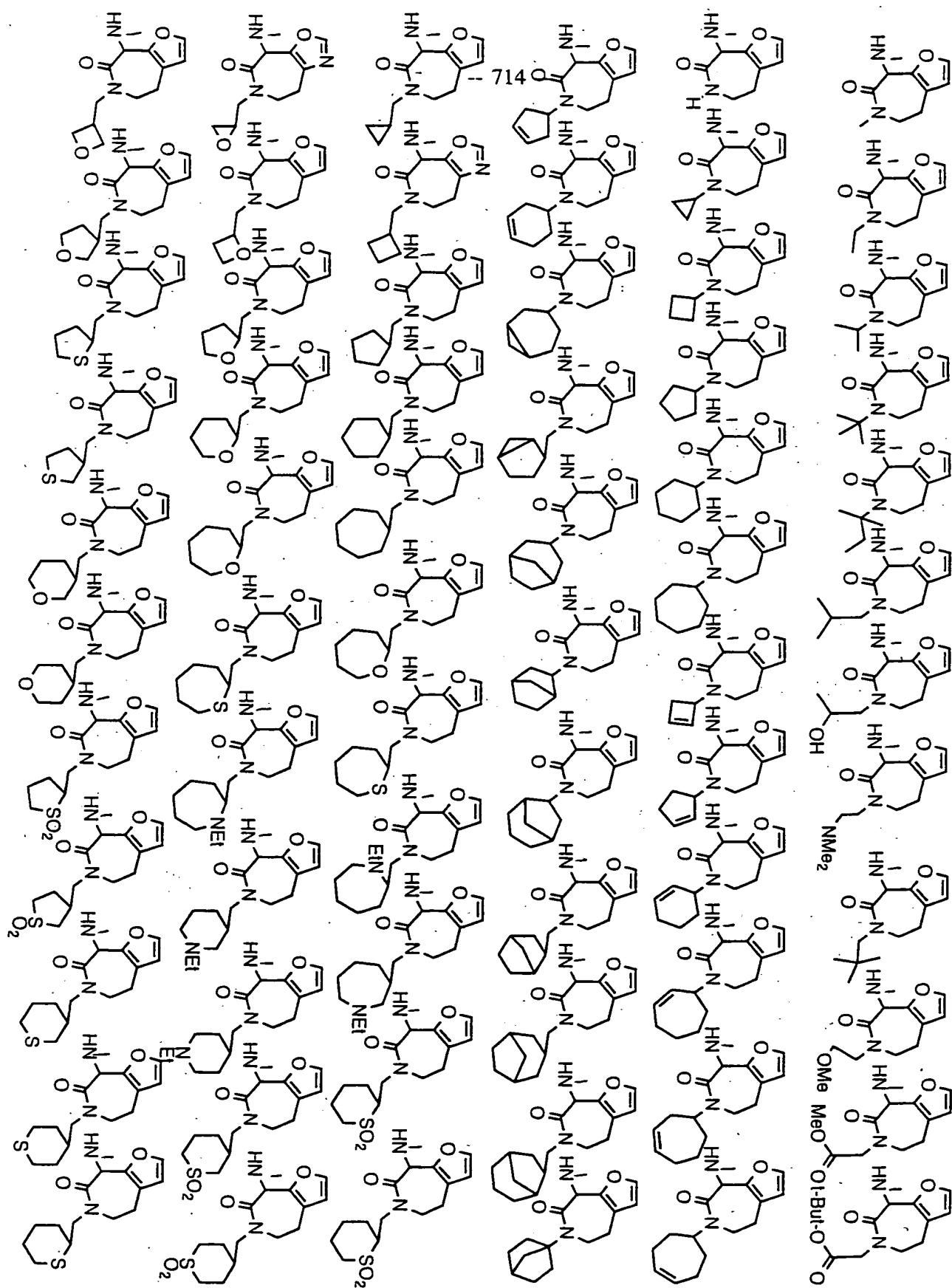


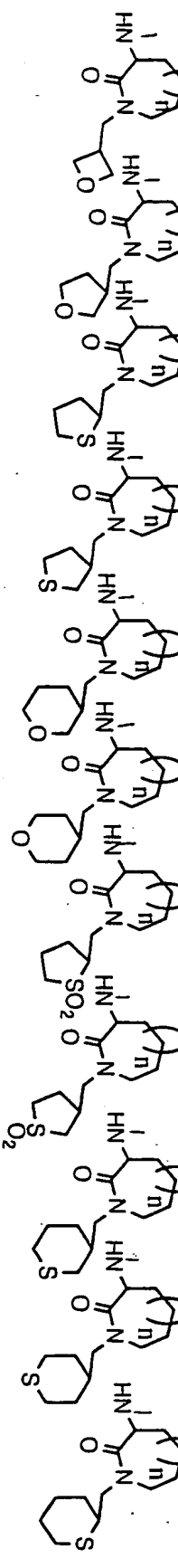
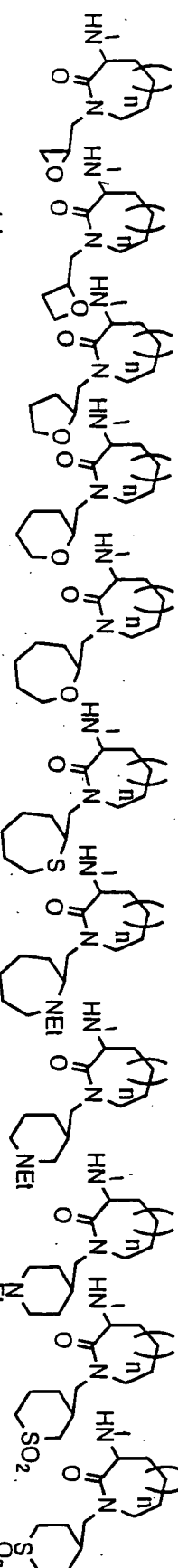
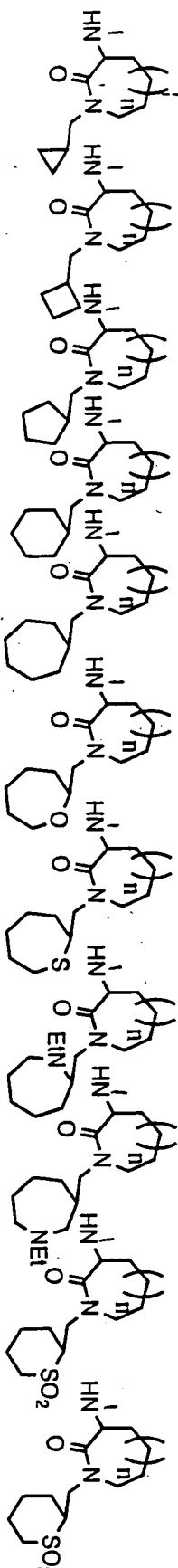
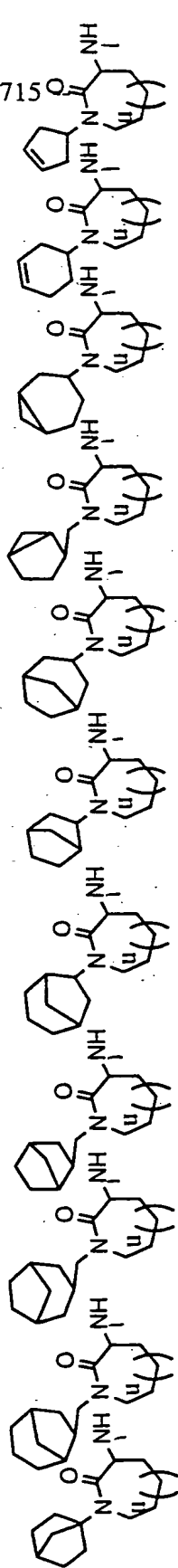
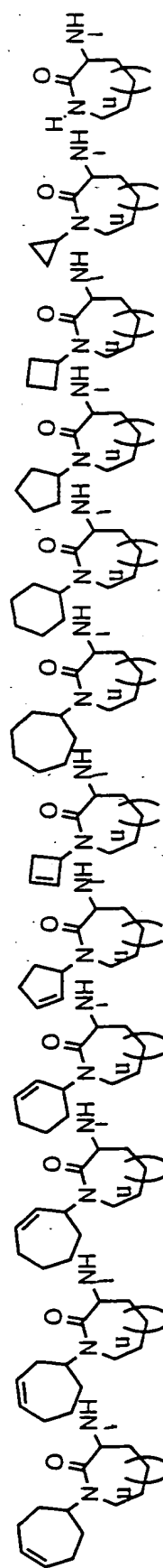
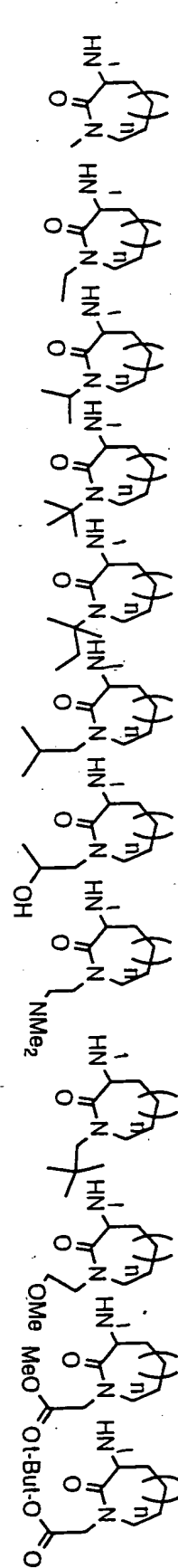


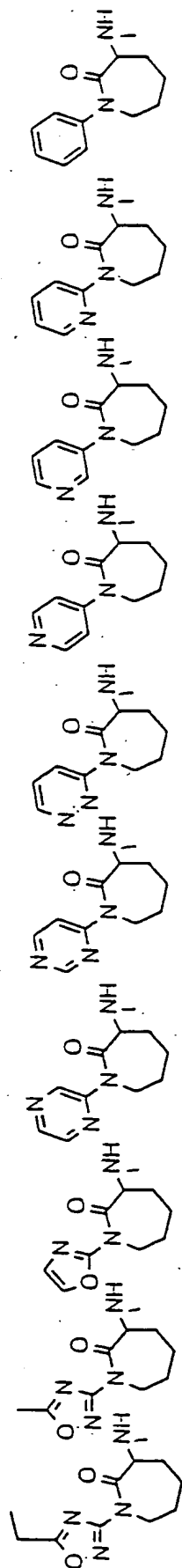
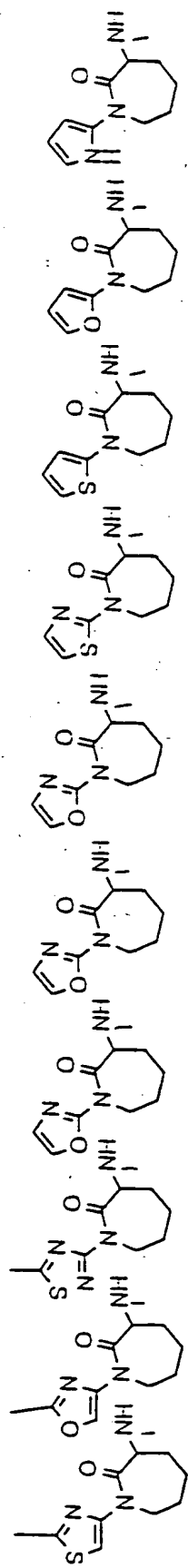
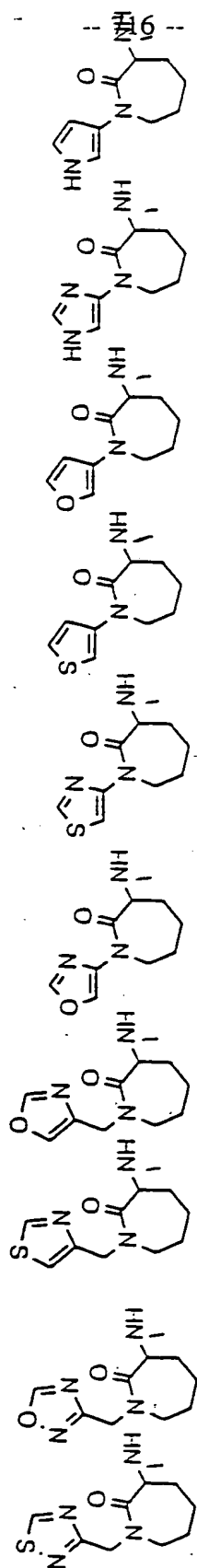
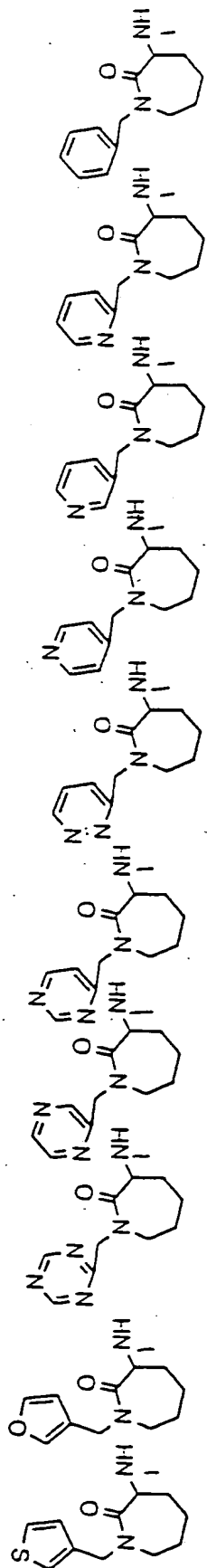
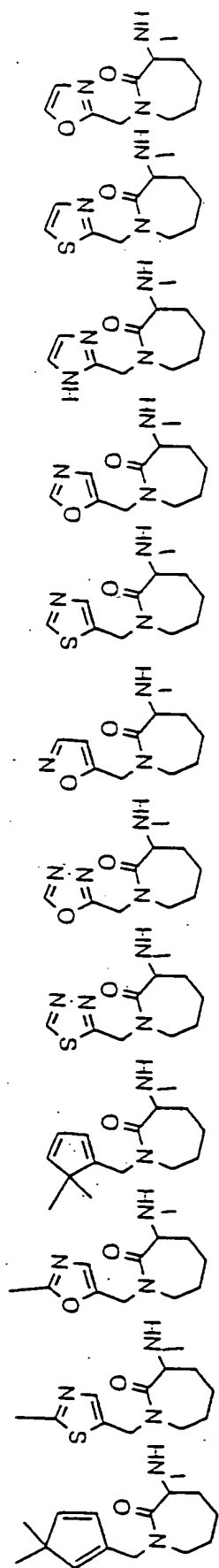


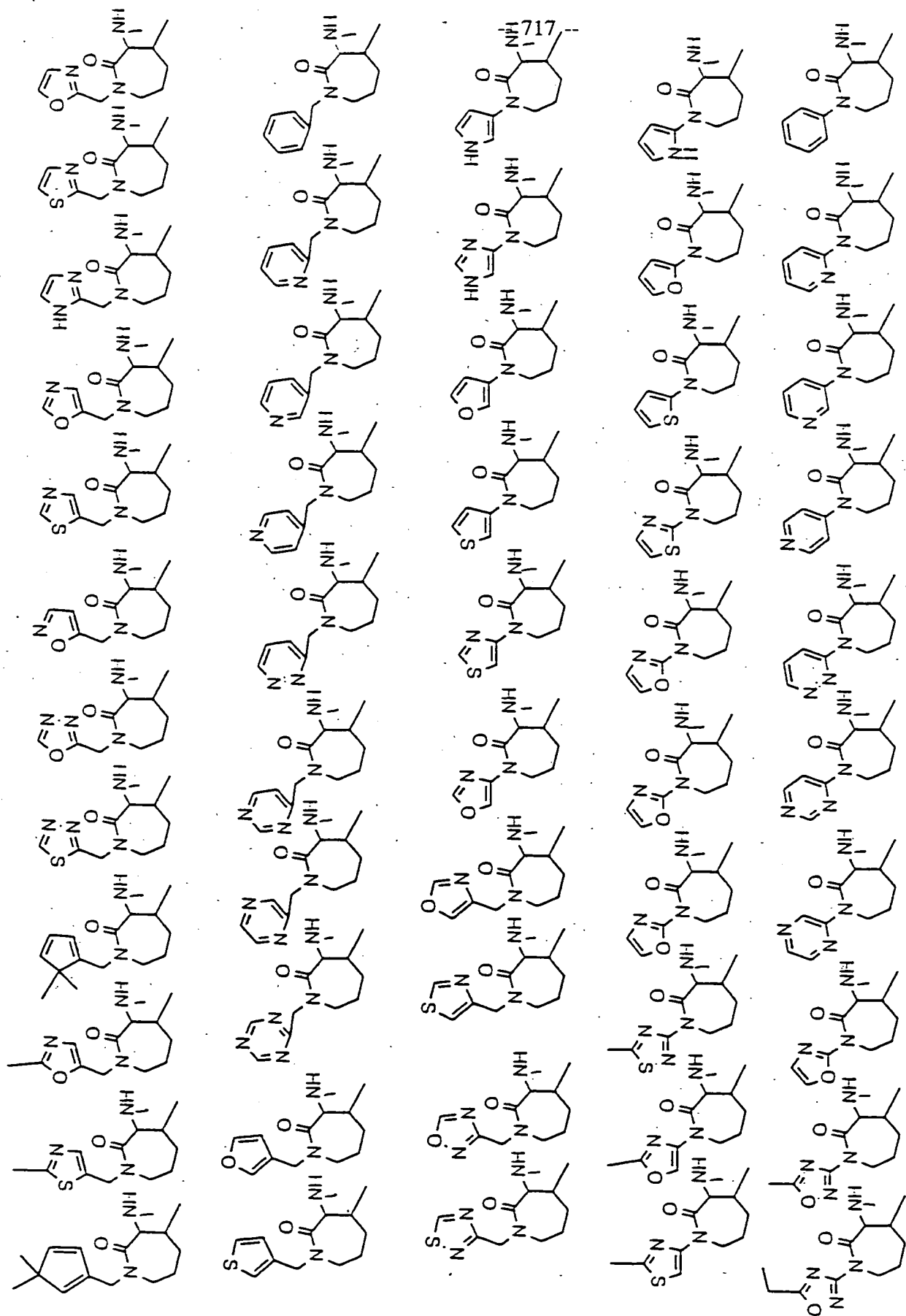


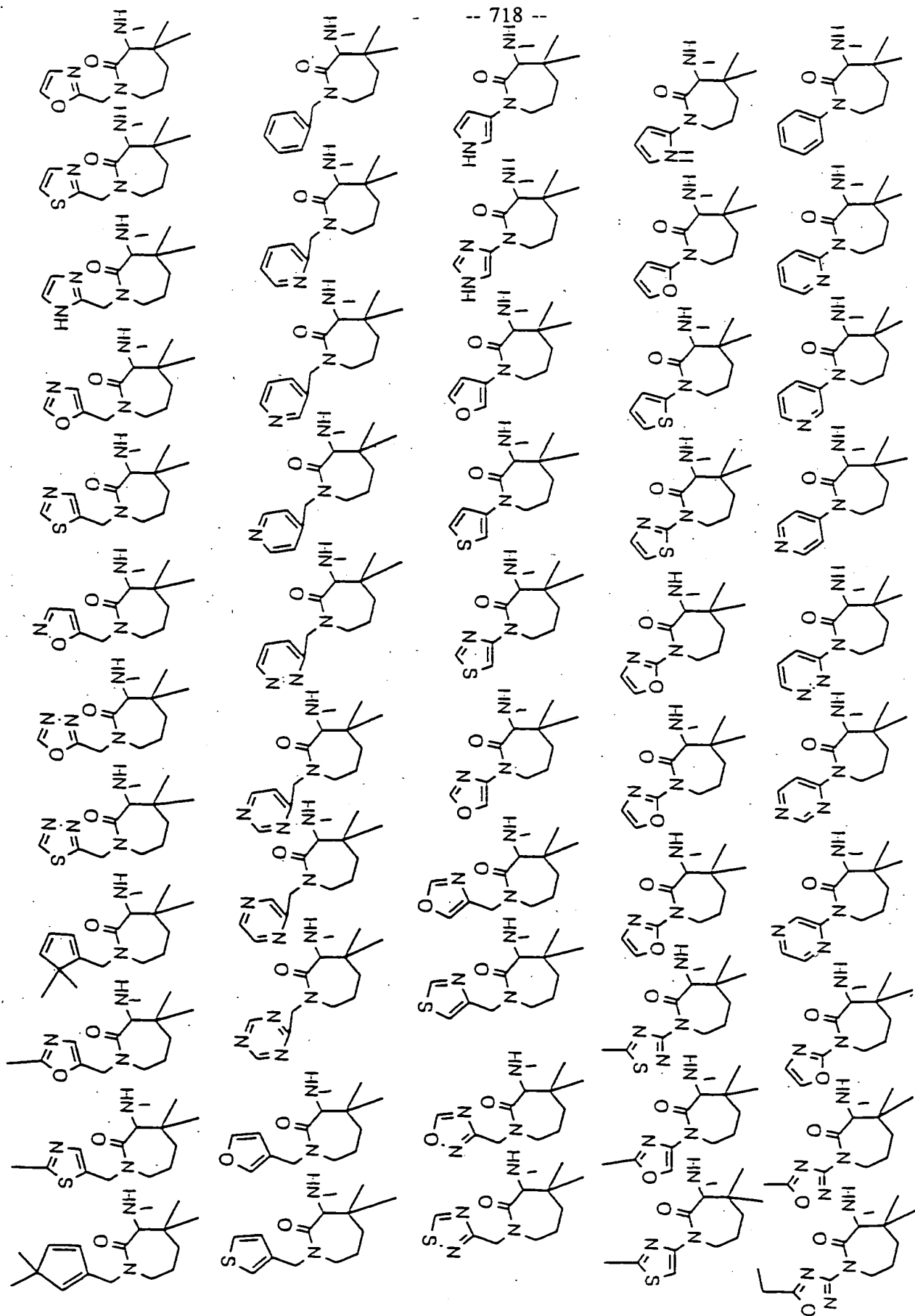


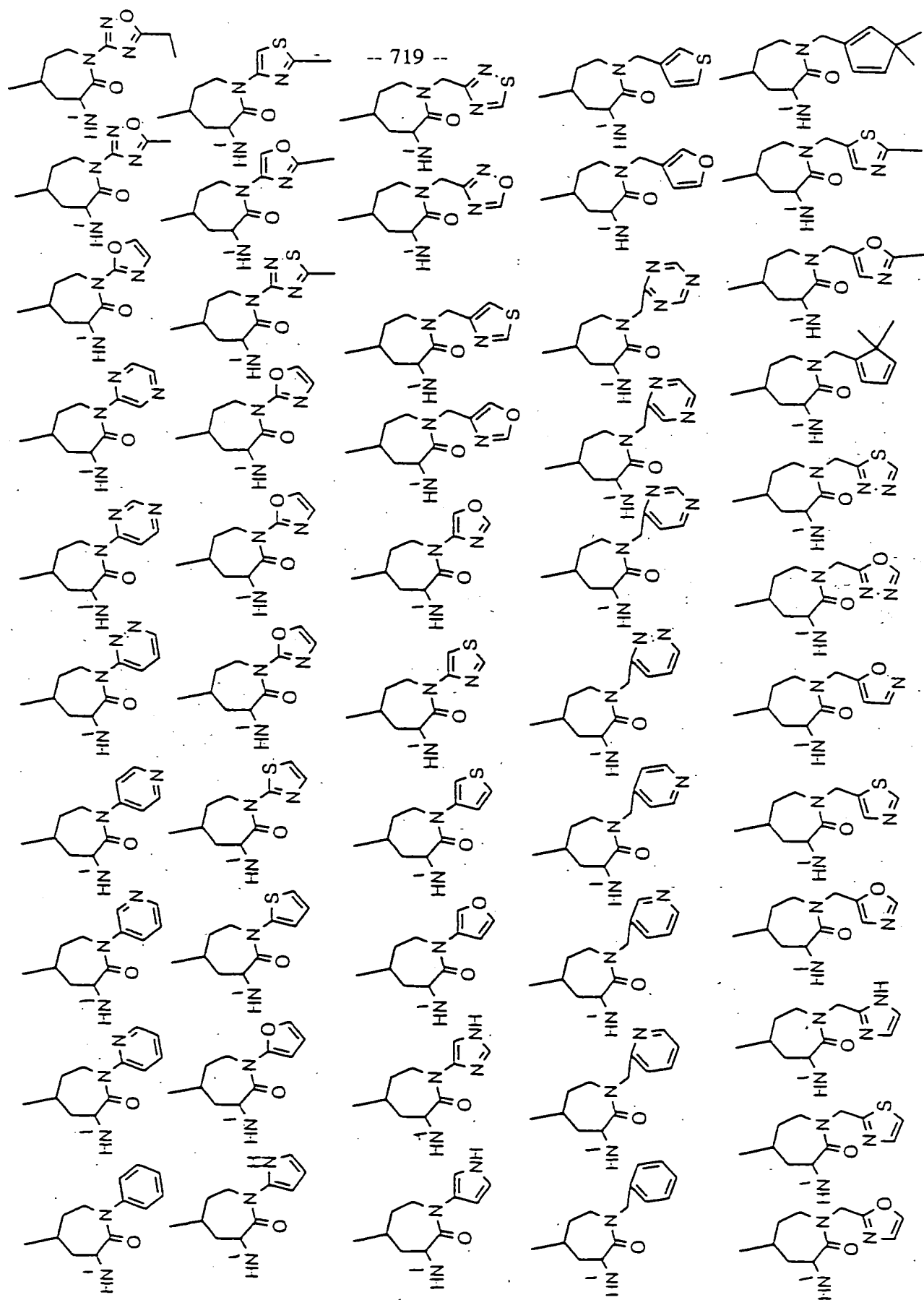


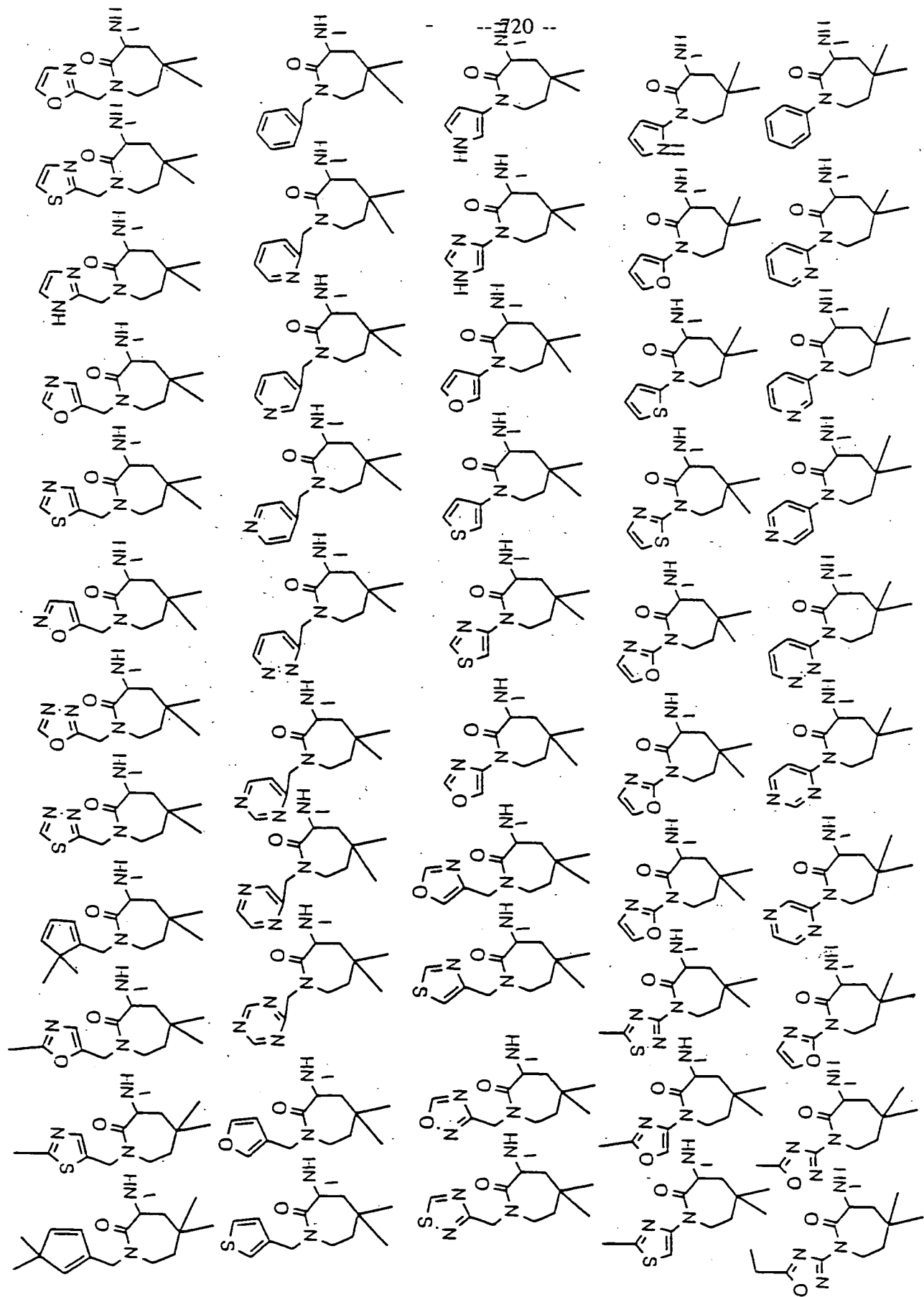


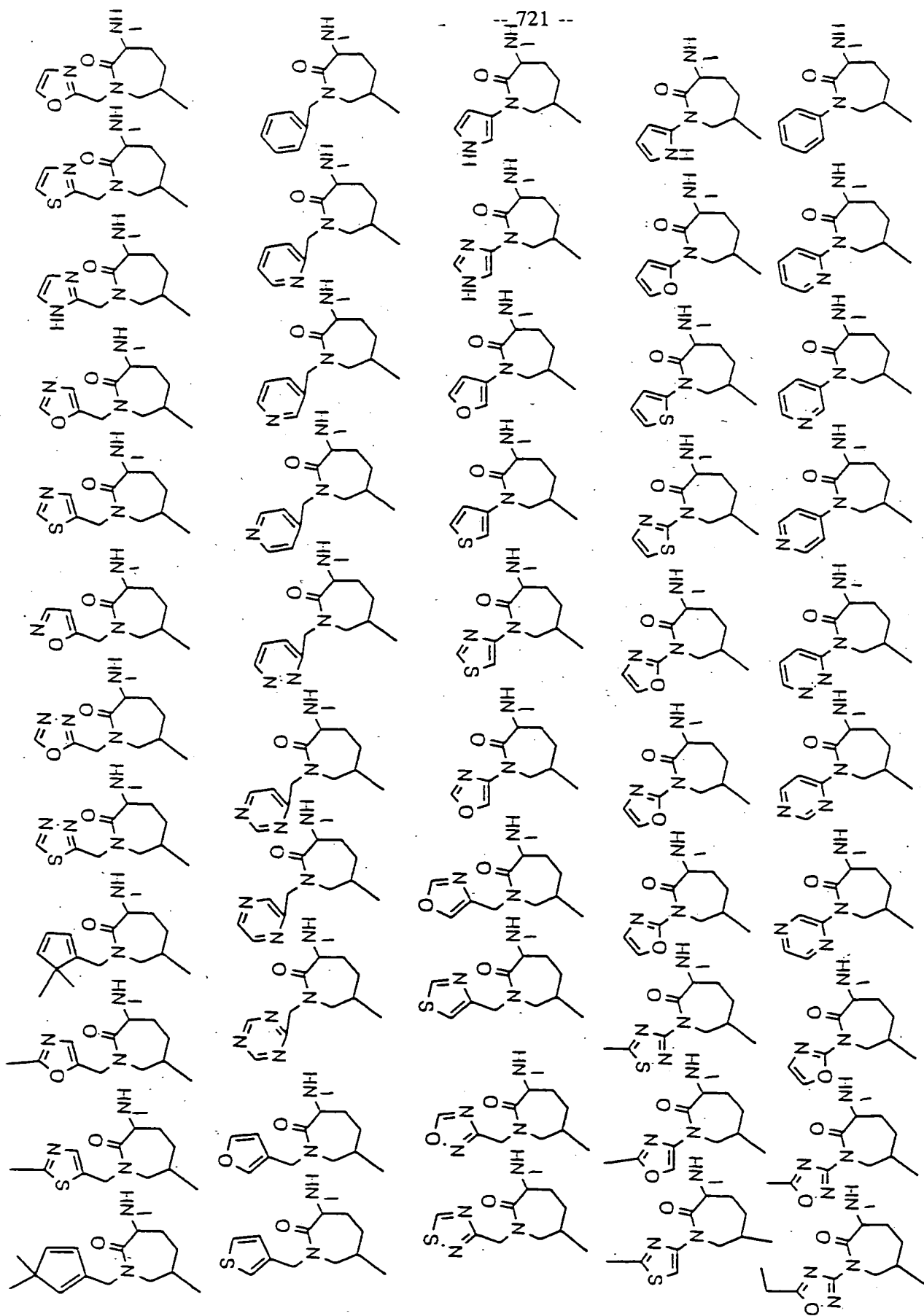


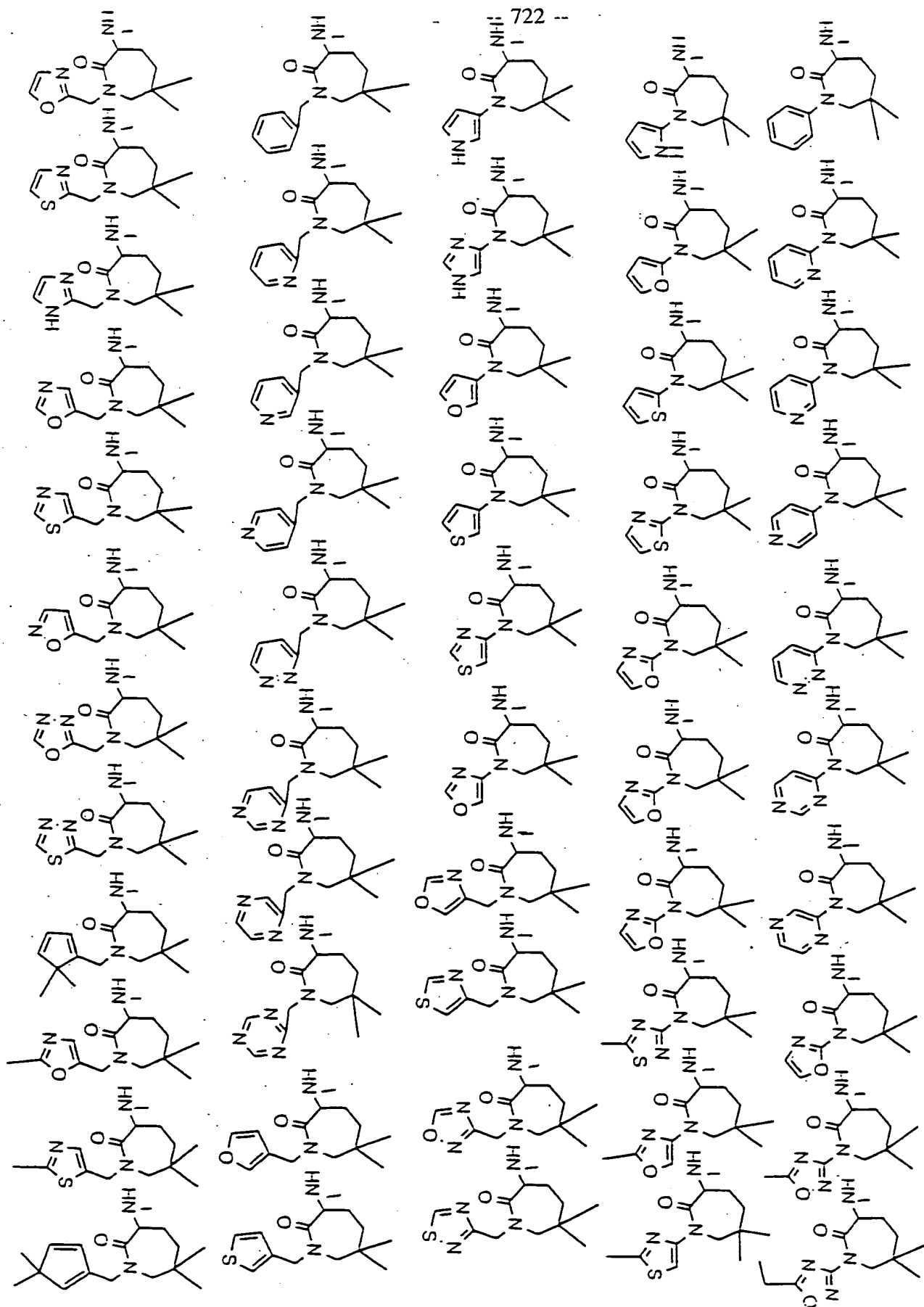


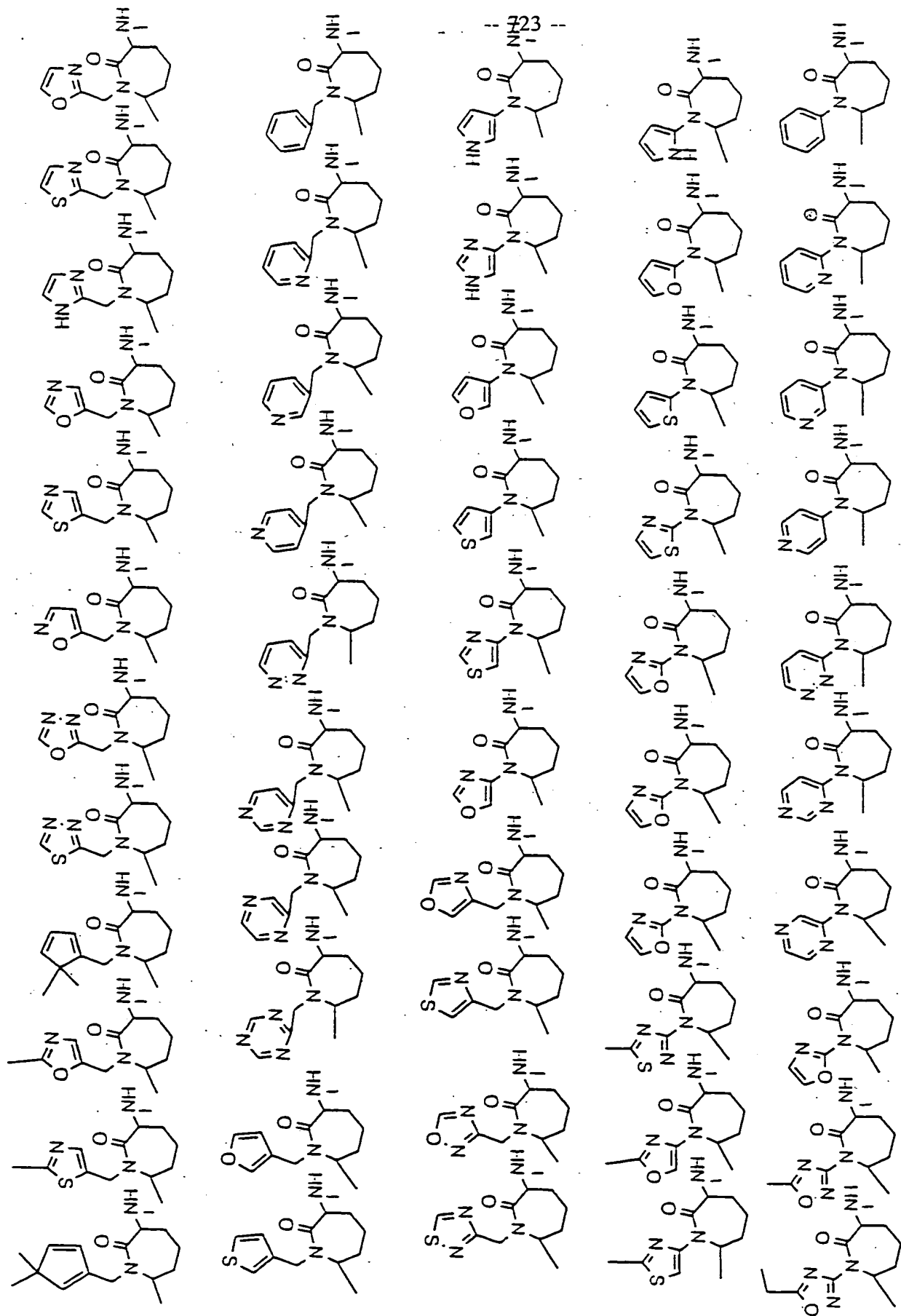


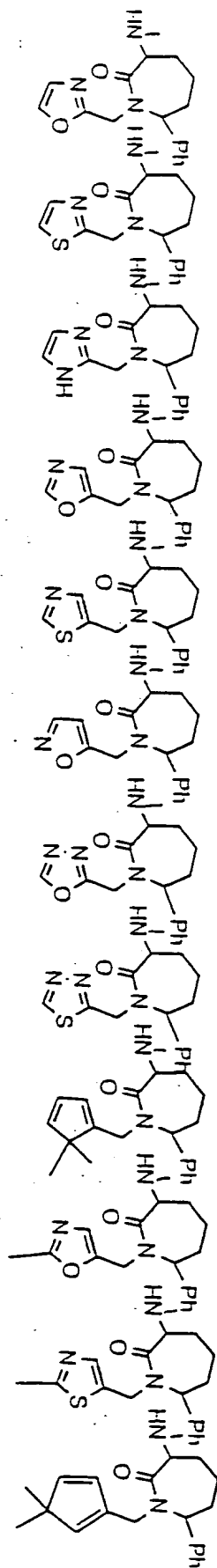
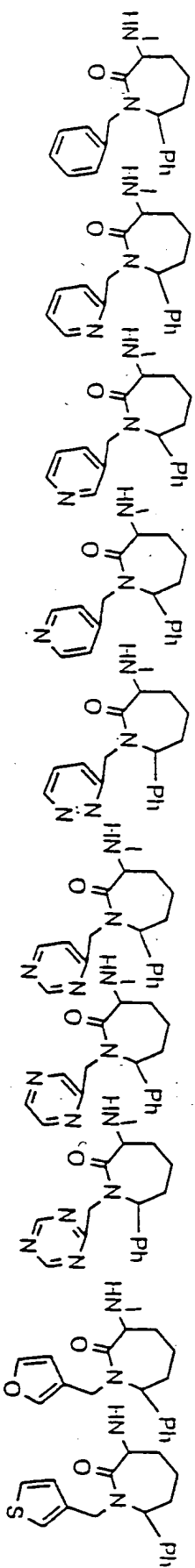
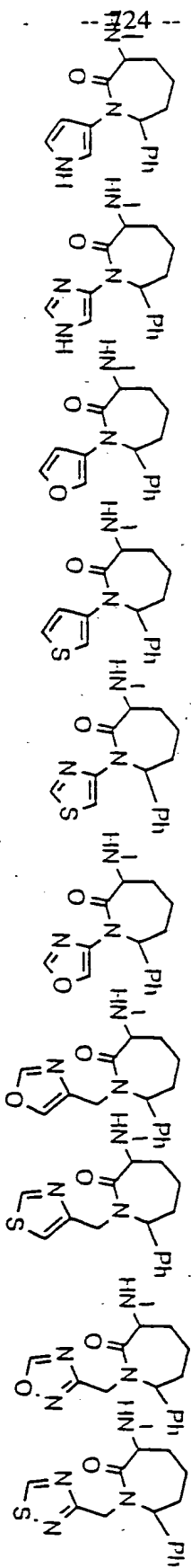
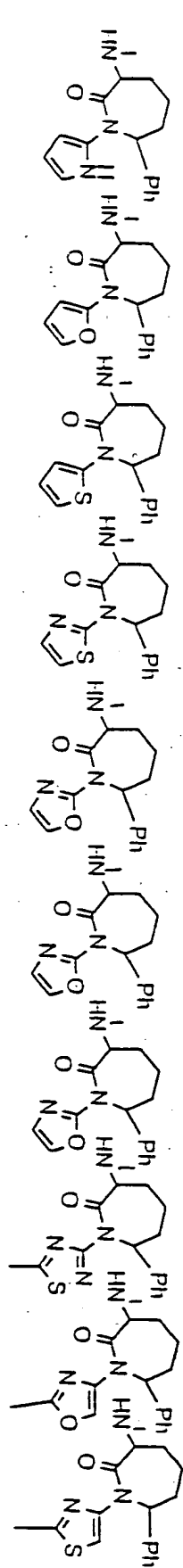
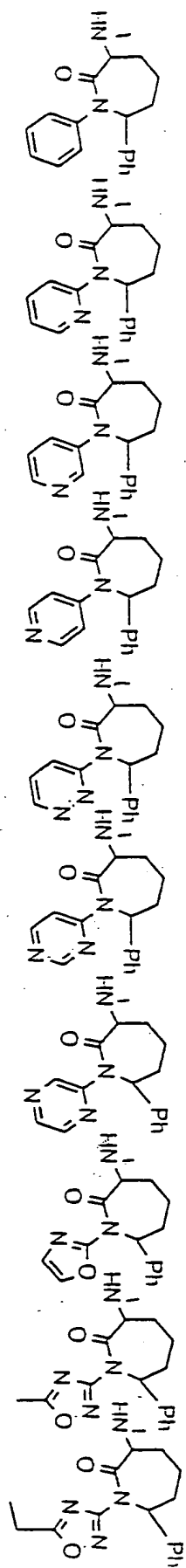


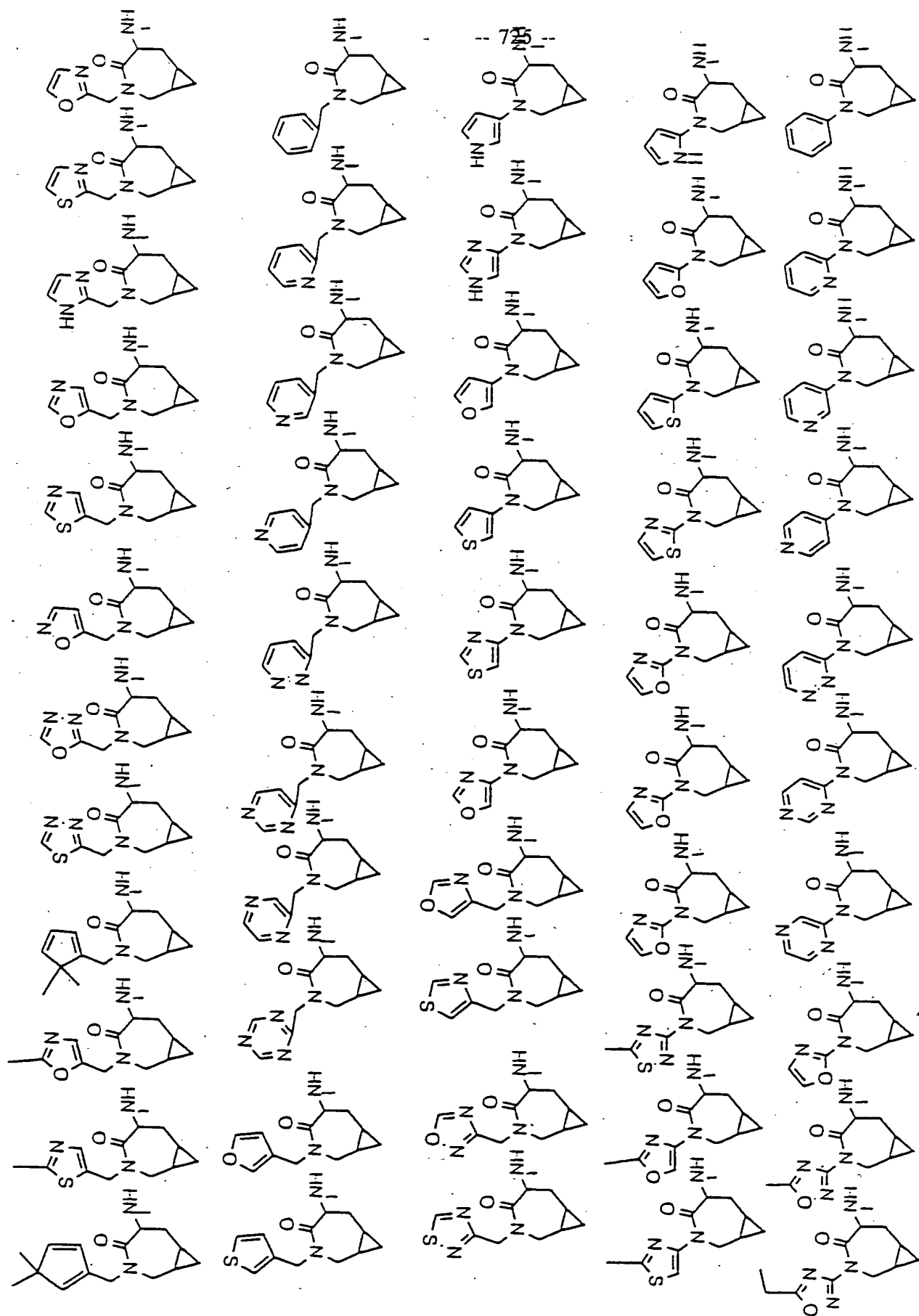


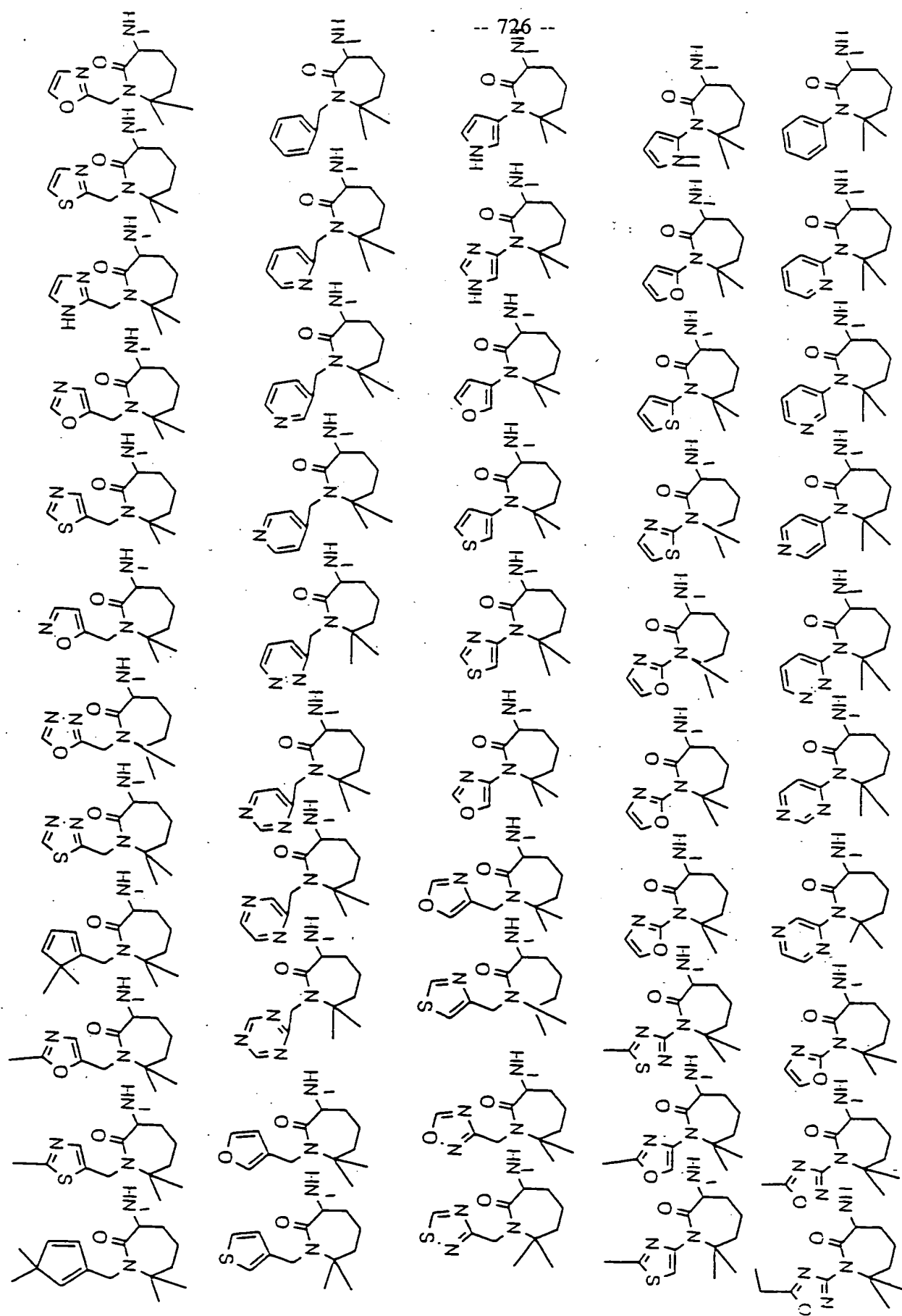


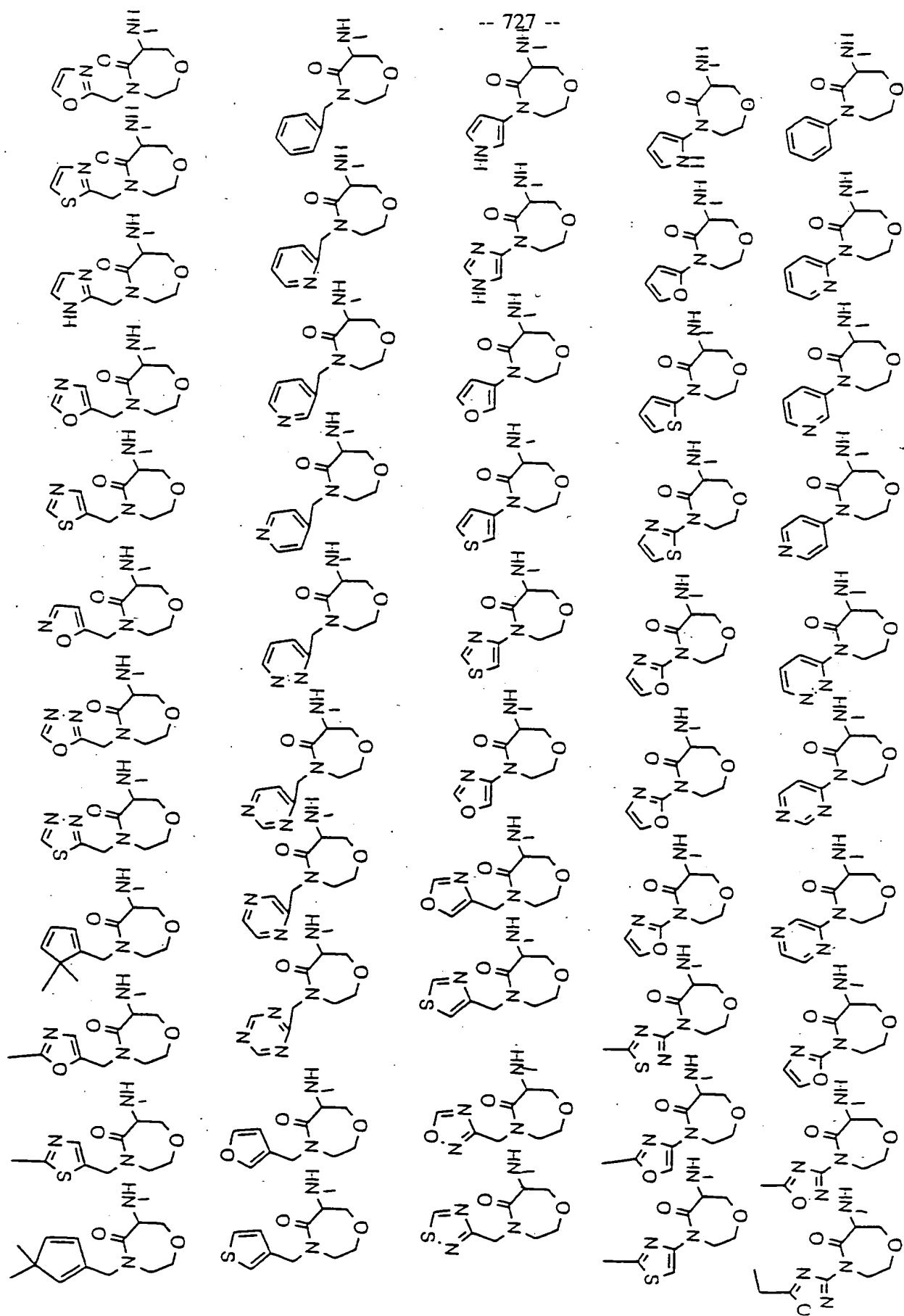


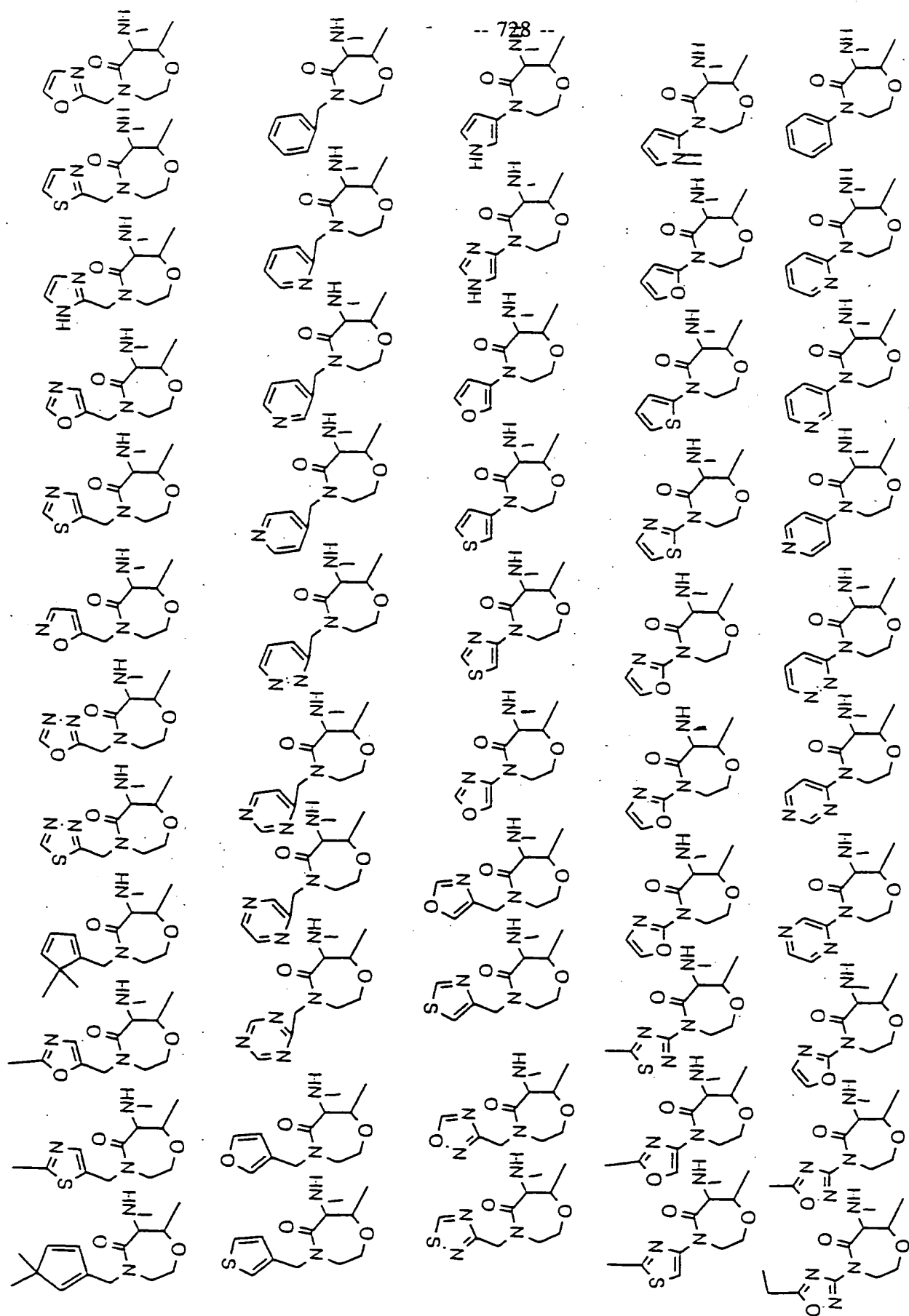


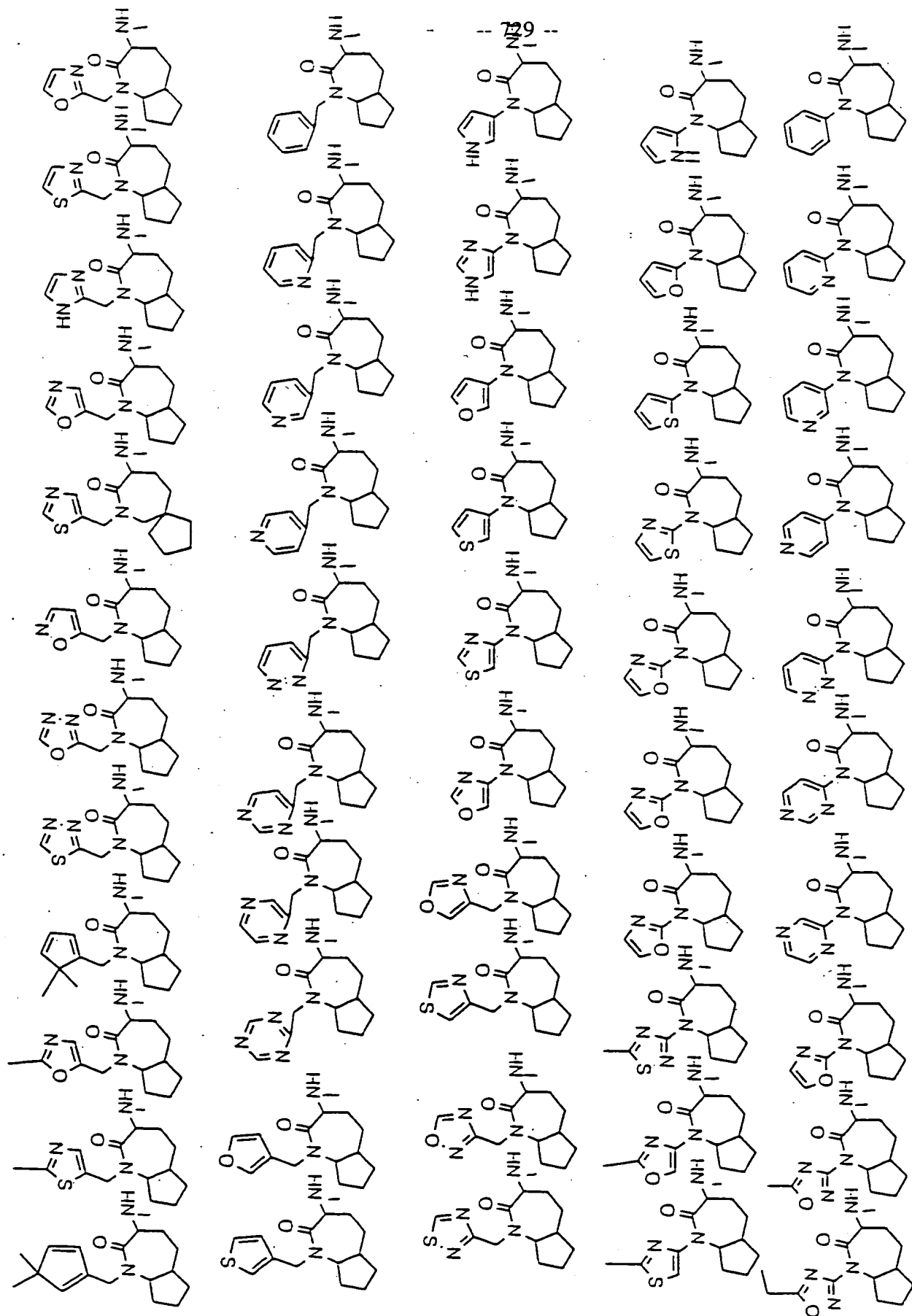


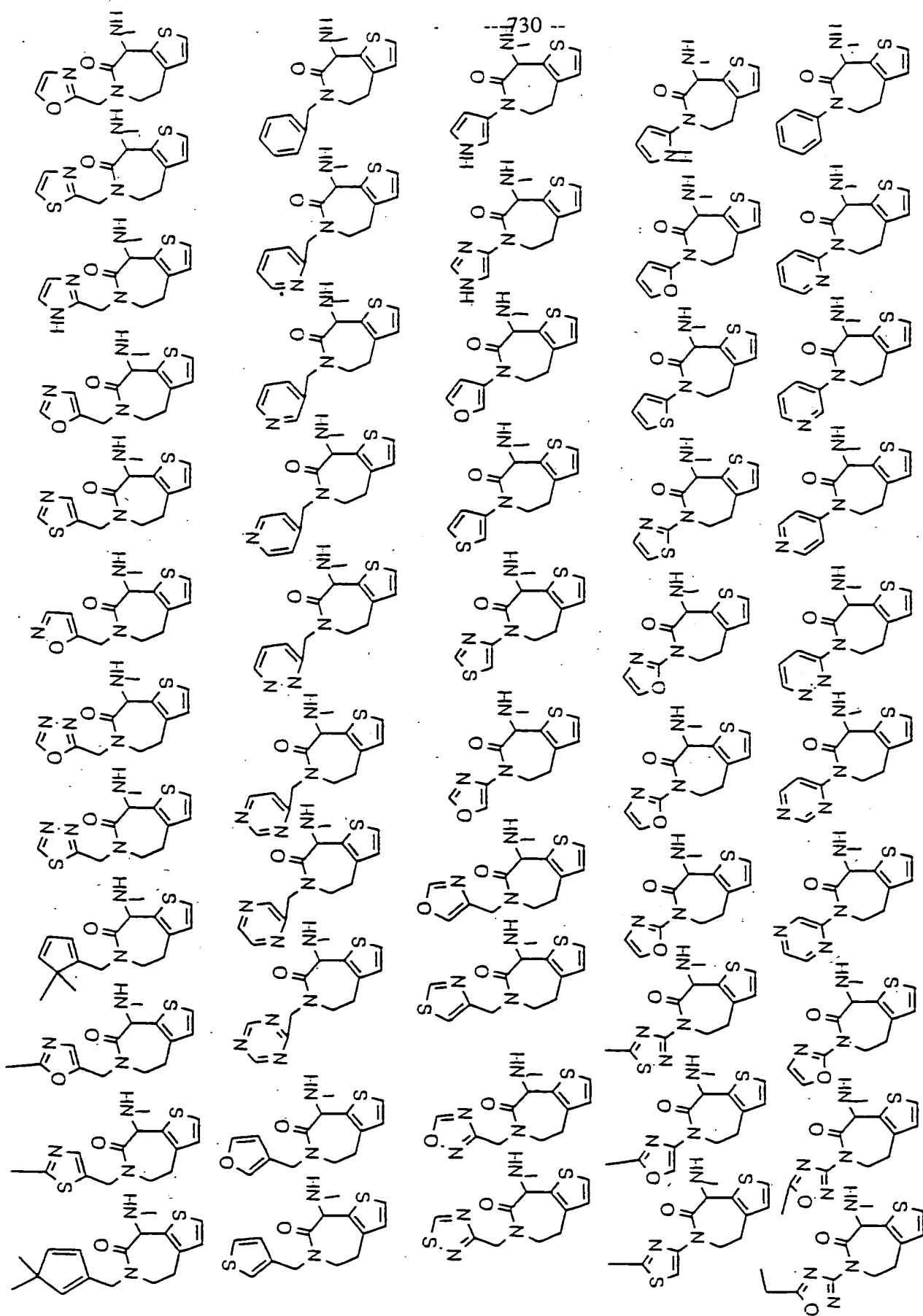


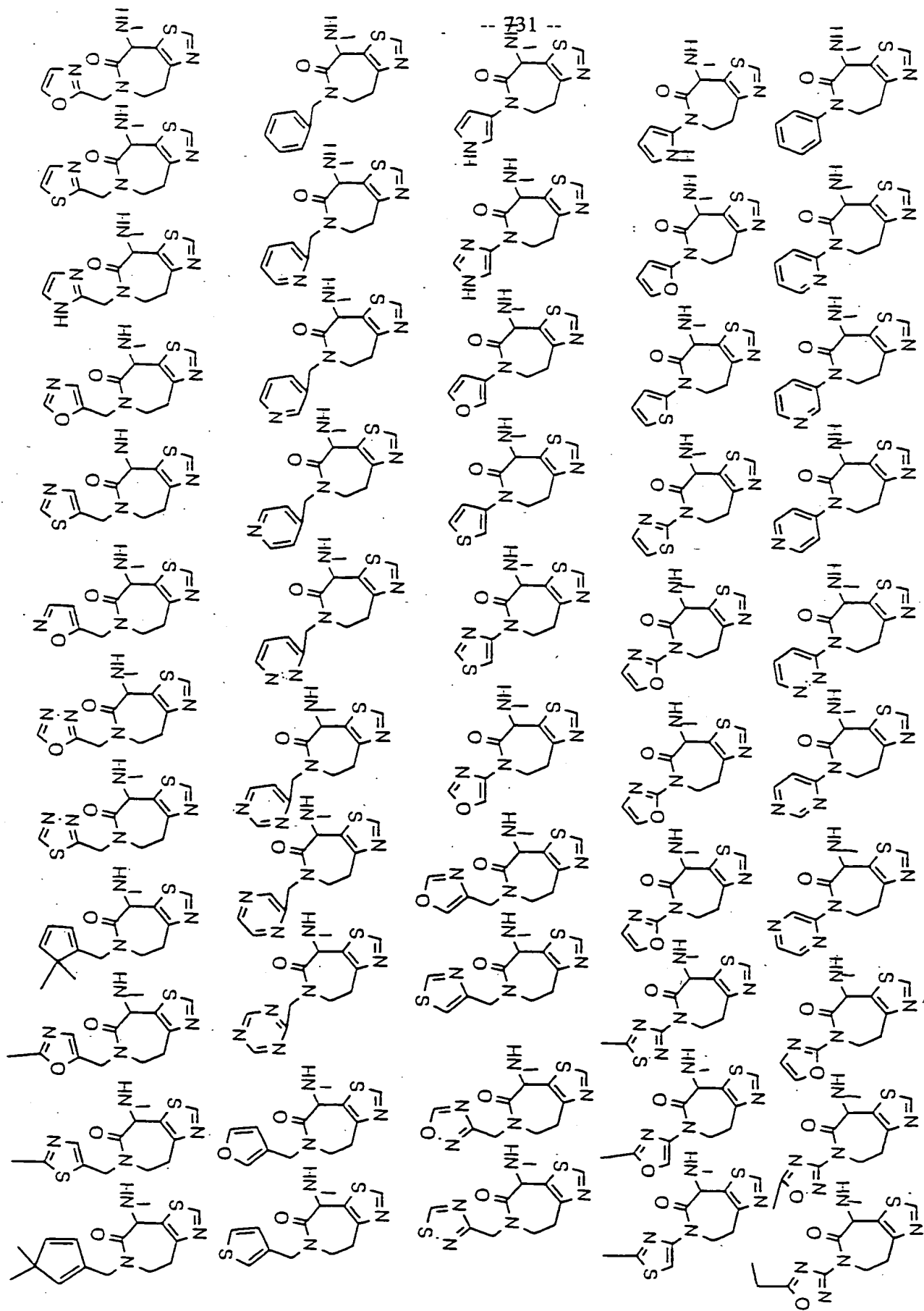


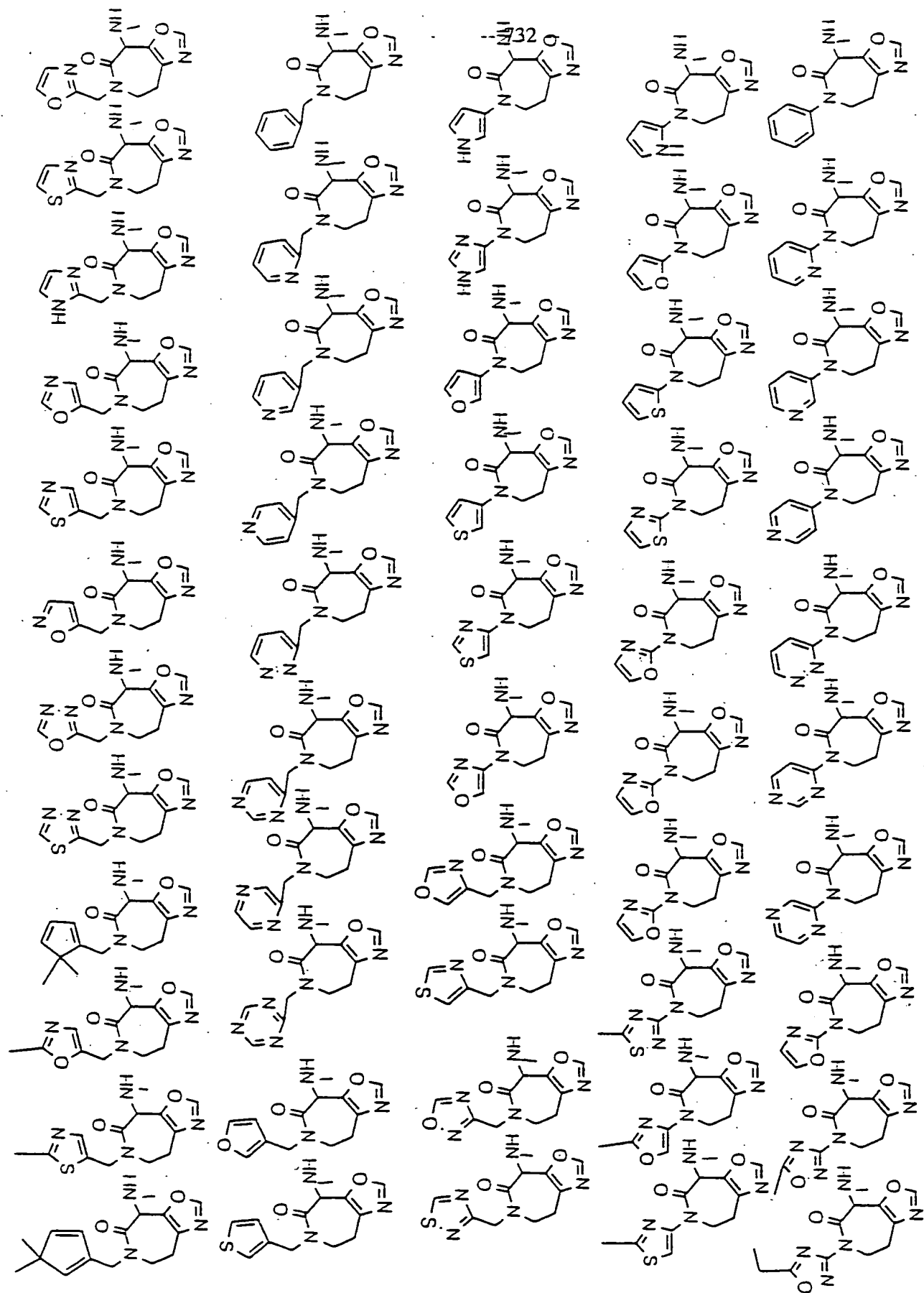


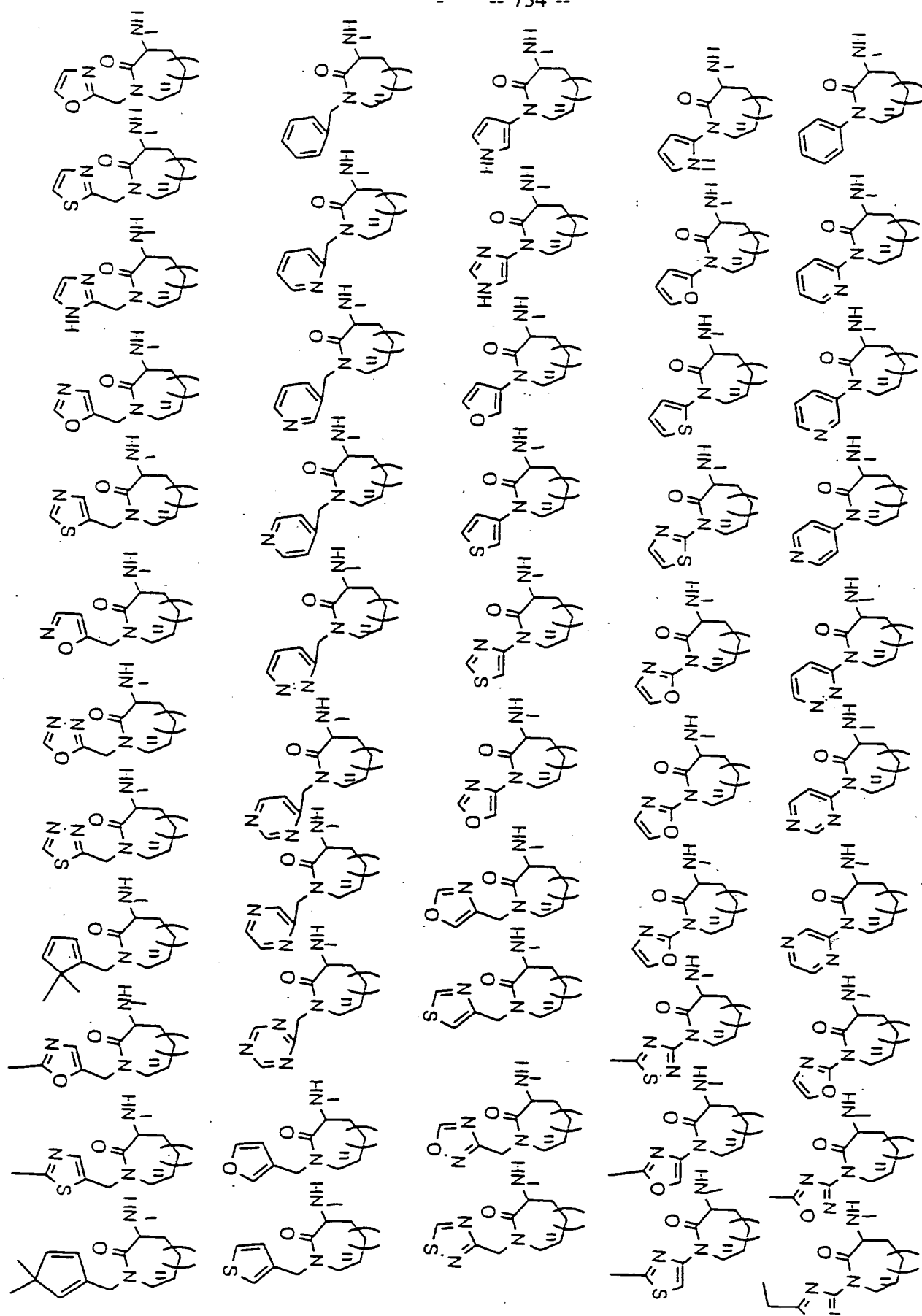











$$n=0, 2, 3, 4$$

Example Bio-1

Cellular Screen for the Detection of Inhibitors of β -Amyloid Production

Numerous compounds of formula I above were assayed for their ability to inhibit β -amyloid production in a cell line possessing the Swedish mutation.

5 This screening assay employed cells (K293 = human kidney cell line) which were stably transfected with the gene for amyloid precursor protein 751 (APP751) containing the double mutation Lys₆₅₁Met₆₅₂ to Asn₆₅₁Leu₆₅₂ (APP751 numbering) in the manner described in International Patent Application Publication No. 94/10569⁸ and Citron et al.¹². This mutation is commonly called
10 the Swedish mutation and the cells, designated as "293 751 SWE", were plated in Corning 96-well plates at 2-4 x 10⁴ cells per well in Dulbecco's minimal essential media (Sigma, St. Louis, MO) plus 10% fetal bovine serum. Cell number is important in order to achieve β -amyloid ELISA results within the linear range of the assay (~0.2 to 2.5 ng per mL).

15

Following overnight incubation at 37°C in an incubator equilibrated with 10% carbon dioxide, media were removed and replaced with 200 μ L of a compound of formula I (drug) containing media per well for a two hour pretreatment period and cells were incubated as above. Drug stocks were
20 prepared in 100% dimethyl sulfoxide such that at the final drug concentration used in the treatment, the concentration of dimethyl sulfoxide did not exceed 0.5% and, in fact, usually equaled 0.1%.

At the end of the pretreatment period, the media were again removed and
25 replaced with fresh drug containing media as above and cells were incubated for an additional two hours. After treatment, plates were centrifuged in a Beckman GPR at 1200 rpm for five minutes at room temperature to pellet cellular debris from the conditioned media. From each well, 100 μ L of conditioned media or appropriate dilutions thereof were transferred into an ELISA plate precoated
30 with antibody 266 [P. Seubert, *Nature* (1992) 359:325-327] against amino acids 13-28 of β -amyloid peptide as described in International Patent Application

Publication No. 94/10569⁸ and stored at 4°C overnight. An ELISA assay employing labelled antibody 3D6 [P. Seubert, *Nature* (1992) 359:325-327] against amino acids 1-5 of β -amyloid peptide was run the next day to measure the amount of β -amyloid peptide produced.

5

Cytotoxic effects of the compounds were measured by a modification of the method of Hansen, et al.¹³. To the cells remaining in the tissue culture plate was added 25 μ L of a 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) (Sigma, St. Louis, MO) stock solution (5 mg/mL) to a final
10 concentration of 1 mg/mL. Cells were incubated at 37°C for one hour, and cellular activity was stopped by the addition of an equal volume of MTT lysis buffer (20% w/v sodium dodecylsulfate in 50% dimethylformamide, pH 4.7). Complete extraction was achieved by overnight shaking at room temperature. The difference in the OD_{562nm} and the OD_{650nm} was measured in a Molecular
15 Device's UV_{max} microplate reader as an indicator of the cellular viability.

The results of the β -amyloid peptide ELISA were fit to a standard curve and expressed as ng/mL β -amyloid peptide. In order to normalize for cytotoxicity, these results were divided by the MTT results and expressed as a
20 percentage of the results from a drug free control. All results are the mean and standard deviation of at least six replicate assays.

The test compounds were assayed for β -amyloid peptide production inhibition activity in cells using this assay. The results of this assay demonstrate
25 that the compounds of formula I inhibit β -amyloid peptide production by at least 30% as compared to control.

Example Bio-2

***In Vivo* Suppression of β -Amyloid Release and/or Synthesis**

30 This example illustrates how the compounds of this invention could be tested for *in vivo* suppression of β -amyloid release and/or synthesis. For these

experiments, 3 to 4 month old PDAPP mice are used [Games et al., (1995) *Nature* 373:523-527]. Depending upon which compound is being tested, the compound is usually formulated at between 1 and 10 mg/mL. Because of the low solubility factors of the compounds, they may be formulated with various vehicles, such as corn oil (Safeway, South San Francisco, CA); 10% ethanol in corn oil; 2-hydroxypropyl- β -cyclodextrin (Research Biochemicals International, Natick MA); and carboxy-methyl-cellulose (Sigma Chemical Co., St. Louis MO).

The mice are dosed subcutaneously with a 26 gauge needle and 3 hours later the animals are euthanized via CO₂ narcosis and blood is taken by cardiac puncture using a 1 cc 25G 5/8" tuberculin syringe/needle coated with solution of 0.5 M EDTA, pH 8.0. The blood is placed in a Becton-Dickinson vacutainer tube containing EDTA and spun down for 15 minutes at 1500 xg at 5°C. The brains of the mice are then removed and the cortex and hippocampus are dissected out and placed on ice.

1. Brain Assay

To prepare hippocampal and cortical tissue for enzyme-linked immunosorbent assays (ELISAs) each brain region is homogenized in 10 volumes of ice cold guanidine buffer (5.0 M guanidine-HCl, 50 mM Tris-HCl, pH 8.0) using a Kontes motorized pestle (Fisher, Pittsburgh PA). The homogenates are gently rocked on a rotating platform for three to four hours at room temperature and stored at -20°C prior to quantitation of β -amyloid.

The brain homogenates are diluted 1:10 with ice-cold casein buffer [0.25% casein, phosphate buffered saline (PBS), 0.05% sodium azide, 20 μ g/ml aprotinin, 5 mM EDTA, pH 8.0, 10 μ g/ml leupeptin], thereby reducing the final concentration of guanidine to 0.5 M, before centrifugation at 16,000 xg for 20 minutes at 4°C. Samples are further diluted, if necessary, to achieve an optimal range for the ELISA measurements by the addition of casein buffer with 0.5 M

guanidine hydrochloride added. The β -amyloid standards (1-40 or 1-42 amino acids) were prepared such that the final composition equaled 0.5 M guanidine in the presence of 0.1% bovine serum albumin (BSA).

5 The total β -amyloid sandwich ELISA, quantitating both β -amyloid (aa 1-40) and β -amyloid (aa 1-42) consists of two monoclonal antibodies (mAb) to β -amyloid. The capture antibody, 266 [P. Seubert, *Nature* (1992) 359:325-327], is specific to amino acids 13 - 28 of β -amyloid. The antibody 3D6 [Johnson-Wood et al., *PNAS USA* (1997) 94:1550-1555], which is specific to amino acids
10 1 - 5 of β -amyloid, is biotinylated and served as the reporter antibody in the assay. The 3D6 biotinylation procedure employs the manufacturer's (Pierce, Rockford IL) protocol for NHS-biotin labeling of immunoglobulins except that 100 mM sodium bicarbonate, pH 8.5 buffer is used. The 3D6 antibody does not recognize secreted amyloid precursor protein (APP) or full-length APP but
15 detects only β -amyloid species with an amino terminal aspartic acid. The assay has a lower limit of sensitivity of ~50 pg/ml (11 pM) and shows no cross-reactivity to the endogenous murine β -amyloid peptide at concentrations up to 1 ng/ml.

20 The configuration of the sandwich ELISA quantitating the level of β -amyloid (aa 1-42) employs the mAb 21F12 [Johnson-Wood et al., *PNAS USA* (1997) 94:1550-1555] (which recognizes amino acids 33-42 of β -amyloid) as the capture antibody. Biotinylated 3D6 is also the reporter antibody in this assay which has a lower limit of sensitivity of ~125 pg/ml (28 pM).

25 The 266 and 21F12 capture mAbs are coated at 10 μ g/ml into 96 well immunoassay plates (Costar, Cambridge MA) overnight at room temperature. The plates are then aspirated and blocked with 0.25% human serum albumin in PBS buffer for at least 1 hour at room temperature, then stored desiccated at
30 4°C until use. The plates are rehydrated with wash buffer (Tris-buffered saline, 0.05% Tween 20) prior to use. The samples and standards are added to the

plates and incubated overnight at 4°C. The plates are washed ≥ 3 times with wash buffer between each step of the assay. The biotinylated 3D6, diluted to 0.5 $\mu\text{g/ml}$ in casein incubation buffer (0.25% casein, PBS, 0.05% Tween 20, pH 7.4) is incubated in the well for 1 hour at room temperature. Avidin-HRP (Vector, Burlingame CA) diluted 1:4000 in casein incubation buffer is added to the wells for 1 hour at room temperature. The colorimetric substrate, Slow TMB-ELISA (Pierce, Cambridge MA), is added and allowed to react for 15 minutes, after which the enzymatic reaction is stopped with addition of 2 N H_2SO_4 . Reaction product is quantified using a Molecular Devices Vmax (Molecular Devices, Menlo Park CA) measuring the difference in absorbance at 450 nm and 650 nm.

2. Blood Assay

The EDTA plasma is diluted 1:1 in specimen diluent (0.2 gm/l sodium phosphate $\cdot\text{H}_2\text{O}$ (monobasic), 2.16 gm/l sodium phosphate $\cdot 7\text{H}_2\text{O}$ (dibasic), 0.5gm/l thimerosal, 8.5 gm/l sodium chloride, 0.5 ml Triton X-405, 6.0 g/l globulin-free bovine serum albumin; and water). The samples and standards in specimen diluent are assayed using the total β -amyloid assay (266 capture/3D6 reporter) described above for the brain assay except the specimen diluent was used instead of the casein diluents described.

Formulations other than those described above can also be used for oral delivery and intravenous delivery to a mammal. For oral delivery, the compound can be mixed with either 100% corn oil or, alternatively, in a solution containing 80% corn oil, 19.5% oleic acid and 0.5% labrafil. The compound can be mixed with the above solutions in concentrations ranging from 1 mg/mL to 10 mg/mL. The compound in solution is preferably administered orally to the mammal at a dose volume of 5 mL/kg of body weight. For IV delivery, the compound is preferably mixed with a solution of 3% ethanol, 3% solutol HS-15 and 94% saline. The compound is preferably mixed with the above solution in concentrations ranging from 0.25 mg/mL to 5 mg/mL. The

compound in solution is preferably administered by IV to the mammal at a dose volume of 2 mL/kg of body weight.

5 From the foregoing description, various modifications and changes in the composition and method will occur to those skilled in the art. All such modifications coming within the scope of the appended claims are intended to be included therein.